



PAN AMERICAN HEALTH ORGANIZATION  
WORLD HEALTH ORGANIZATION



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### VACCINES AND IMMUNIZATION

This report updates the Executive Committee on the progress being made by Member States in the area of vaccines and immunization. The document makes a special call to all countries to take a proactive approach to achieve measles eradication by the year 2000. It will be critical to implement PAHO's recommended vaccination strategy for measles eradication in full. This will include targeting for vaccination of other groups potentially at high-risk for measles, such as health care workers, college and university students and faculty, military personnel, and people working in the tourist industry.

In support of this goal and the control of other vaccine-preventable diseases, the area of national surveillance systems will demand sustained and systematic attention in the years to come, in order to support the effective implementation of current immunization programs and to introduce other vaccines of public health importance in the routine vaccination schedule.

The report also calls the attention of Member States to the possible impact of decentralization on immunization programs. The shift in decision-making and resource allocation to local entities poses a formidable task for the uniform delivery of immunization programs to all areas of a country. Member States need to clarify the roles of central and local governments and ensure that technical and managerial capabilities are in place at the local level, especially to conduct surveillance and immunization activities.

The Executive Committee is requested to review this document and make recommendations to the Secretariat on how it might accelerate the progress in the Region of the Americas in the area of vaccines and immunization.

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## 1. Introduction

Collaboration with the countries in the Region of the Americas emphasizes the delivery of quality and equitable vaccination programs supported by an effective surveillance and laboratory infrastructure. The Division of Vaccines and Immunization (HVP) pays special attention to adapting its technical cooperation with countries to an environment in which the process of decentralization is ongoing.

Key is the need to ensure that capabilities are in place to conduct surveillance activities at the periphery. PAHO has developed a set of sustainability indicators that were endorsed by all countries at the 12th Meeting of the Technical Advisory Group on Vaccine Preventable Diseases (TAG) in 1997, to monitor coverage, surveillance data, and resource allocation for vaccine-preventable diseases at the district level. The data coming from these indicators is being used to prioritize immunization interventions and to measure the impact of the decentralization and health reform processes.

The information obtained has been a valuable tool for managers of national immunization programs. At the regional level it has enabled PAHO to highlight priority countries and under-served populations within countries, in order to plan equitable vaccination programs. Recently, efforts have been focused on the integration of national laboratory and epidemiology units, which is resulting in more streamlined and efficient case handling, from investigation to final classification.

Another area of the Program's technical cooperation with countries has centered on sustainable ways to introduce vaccines in the routine immunization schedule against other vaccine-preventable diseases of public health importance, such as rubella and congenital rubella syndrome, hepatitis B, *Haemophilus influenzae* type b, and yellow fever. PAHO is currently advising countries on how to build a surveillance, laboratory and logistical infrastructure, including cold chain, to accommodate the introduction of these vaccines. The surveillance systems established for measles and poliomyelitis will serve as a foundation to build these new systems. These developments have expanded the role of PAHO's Revolving Fund for Vaccine Procurement, in an effort to accelerate the incorporation of additional vaccines.

During 1998, the Heads of States of the Americas endorsed the initiative "Health Technology Linking the Americas." One of its components is the Regional Vaccine Initiative, which calls for partnerships among countries in the Region and international organizations in vaccine research, development and production; epidemiological surveillance for vaccine-preventable diseases; and laboratory diagnosis. The endorsement of the Regional Vaccine Initiative has placed PAHO's technical cooperation with countries in the area of immunization and vaccines at the highest political level. This dialogue

represents an important step to gather the necessary national and international expertise to implement effective public health responses. Under the framework of the Regional Vaccine Initiative, PAHO will strengthen its catalytic role in facilitating and promoting the establishment of priority inter-institutional and inter-country projects that will speed up the process of research, development and production of conjugated vaccines. The area of polysaccharide-protein conjugated vaccines has been selected due to its potential application in the development of other bacterial vaccines with a known impact on childhood diseases, such as *Haemophilus influenzae* type b, meningococcal and pneumococcal.

The collaboration of PAHO with the First Ladies of the Americas has also continued, working towards eradicating measles from the Americas by the year 2000. New partnership agreements have been prepared with the World Bank on a project to improve the sustainability of Bolivia's immunization program and to insure the introduction of other vaccines in the country's routine schedule, and with the Centers for Disease Control and Prevention (CDC) to strengthen measles and rubella surveillance in the Americas.

## **2. Decentralization**

The Program has started to monitor the impact of health reform and decentralization on the delivery of immunization programs, through its performance evaluations of national immunization programs. Initial assessments indicate that most countries are going through a transition period, as they put in place new decentralized financial and administrative systems to manage their immunization programs. While laws have been enacted that transfer decision-making and resources to the local levels, in practice there is a need to spell out the responsibilities of the various institutions assigned to the delivery of immunization services, as well as mechanisms to transfer and manage resources. These changes have caused delays, especially in the allocation of resources for routine vaccination activities and for emergency outbreak situations in some countries. In this context, countries should also make every effort to establish laws that ensure national financing of recurrent costs of vaccines and other inputs.

## **3. Emerging Partners in Immunization**

The Program has started to monitor more systematically emerging partners within countries, such as pediatric and infectious diseases associations, private insurance groups, and private voluntary organizations, in an effort to determine avenues for formal joint collaboration in national surveillance and immunization activities. For example, a meeting was sponsored by PAHO in Honduras with the participation of public health authorities and the private medical sector (pediatric societies) of Central America, to

ensure the latter's inclusion in surveillance and immunization activities. The meeting resulted in commitments for the private sector to participate actively in surveillance activities of vaccine-preventable diseases.

#### **4. Progress to Date**

##### **4.1 *Vaccination Coverage***

Overall regional DPT vaccine coverage in 1998 was 88%; 19 of 39 reporting countries (49%) had coverage of  $\geq 90\%$ . The following countries reported DPT3 coverage less than 80%: Bolivia (76%), Colombia (70%), Dominican Republic (74%), and Venezuela (38%) (see Table 1).

Overall regional OPV3 vaccine coverage in 1998 was 91%; 21 of 39 reporting countries (54%) had coverage of  $\geq 90\%$ . The following countries reported OPV3 coverage less than 80%: Bolivia (75%), Colombia (72%), Dominican Republic (73%), and Venezuela (64%).

Overall regional BCG vaccine coverage in 1998 was 99%; 18 of 35 reporting countries (51%) had coverage of  $\geq 90\%$ .

Overall regional measles vaccine coverage in 1998 was 87%; 22 of 39 reporting countries (56%) had coverage of  $\geq 90\%$ . The only country reporting under 80% was Colombia (75%).

##### **4.2 *Measles Eradication by the Year 2000***

More than four years have passed since the goal of eradicating measles from the Americas was established at the 24th Pan American Sanitary Conference (September 1994). The majority of the countries in the Americas continue to successfully control measles and prevent large outbreaks with PAHO's recommended vaccination strategy for measles eradication. While great progress has been made towards achieving this goal, with a marked reduction in the annual number of reported cases, measles virus continues to circulate in a few countries of the Region (see Figure 1).

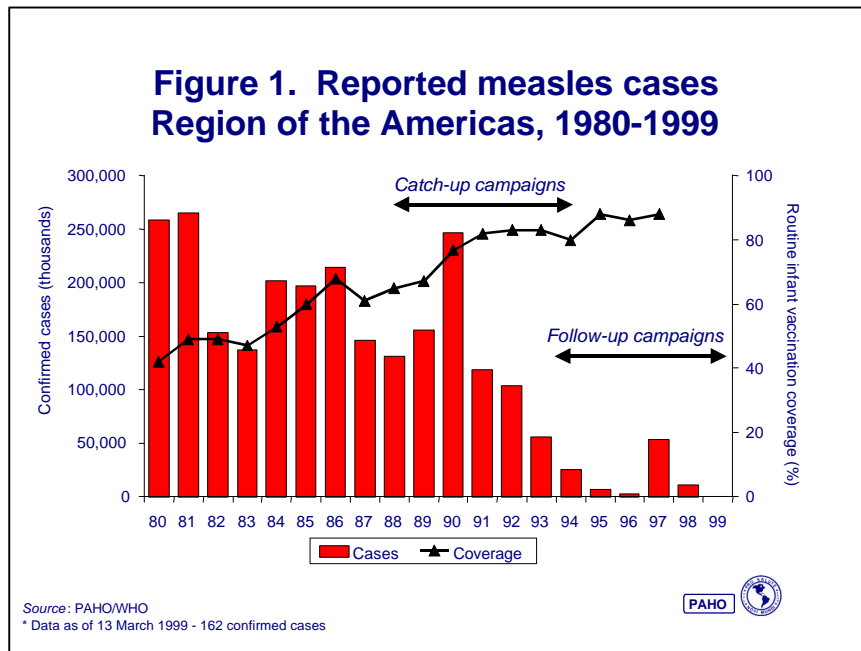
The ramifications of the measles outbreak in southern Brazil in late 1997, with over 52,284 confirmed cases, continue to affect Bolivia and countries of the Southern Cone, particularly Argentina and Paraguay. For 1998, the provisionally confirmed cases in the Region of the Americas total 12,940, which represents a 76% reduction in measles cases when compared to confirmed cases in 1997. The measles outbreaks in Brazil and Argentina in 1997 and 1998 have again demonstrated the lethality of measles virus. Over

**Table 1. Vaccination Coverage, Region of the Americas, 1998**

Region/Country	DPT	OPV	Measles	BCG
<b>Andean</b>				
Bolivia	76	75	80	85
Colombia	70	72	75	82
Ecuador	85	83	88	98
Peru	98	96	93	96
Venezuela	38	64	94	80
<b>Brazil</b>	94	96	96	99
<b>Central America</b>				
Belize	93	94	88	...
Costa Rica	...	...	...	...
El Salvador	99	99	98	99
Guatemala	89	91	81	88
Honduras	96	96	97	96
Nicaragua	86	91	99	91
Panama	98	99	95	99
<b>English-Speaking Caribbean</b>				
Anguilla	99	99	96	99
Antigua & Barbuda	99	99	99	n/a
Bahamas	...	...	...	...
Barbados	...	...	...	...
Cayman Islands	...	...	...	...
Dominica	...	...	...	...
Grenada	97	95	97	n/a
Guyana	90	90	93	92
Jamaica	85	85	85	87
Montserrat	99	99	99	99
St. Christopher & Nevis	98	98	99	99
St. Lucia	88	88	90	85
St. Vincent & Grenadines		99	99	99
Suriname	90	90	82	n/a
Trinidad & Tobago	91	91	90	n/a
Turks & Caicos	99	99	99	99
British Virgin Islands	99	99	99	95
<b>Latin Caribbean</b>				
Cuba	99	97	99	99
Dominican Republic	74	73	95	86
Haiti	...	...	...	...
<b>Mexico</b>	96	96	96	99
<b>North America</b>				
Bermuda	...	...	...	...
Canada*	97	...	96	...
<b>United States*</b>	<b>95</b>	<b>91</b>	<b>91</b>	<b>...</b>
<b>Southern Cone</b>				
Argentina	83	88	99	99
Chile	...	...	...	...
Paraguay	...	...	...	...
Uruguay	87	87	86	99
<b>TOTAL*</b>	<b>88</b>	<b>91</b>	<b>87</b>	<b>99</b>

\* Provisional total based on countries reporting, excluding Canada and the United States of America  
n/a - Data not applicable  
... Data not available Source: PAHO Date updated: 5 April 1999

100 measles-related deaths have been reported in the past two years in both countries, most occurring among unvaccinated infants and preschool-aged children. A factor contributing to the resurgence of measles in Brazil and Argentina was the failure to fully implement the measles eradication strategy. Once measles virus was re-introduced into these areas, it was virtually impossible to stop it by rapidly implementing emergency measles vaccination (see Table 2).



These outbreaks reiterate the extreme infectivity of measles virus and the importance of achieving and maintaining high measles immunity in infants and preschool-aged children, especially those living in urban environments. Experience in the Americas is showing that the high population density of cities greatly facilitates measles virus circulation between infected and susceptible individuals, especially when the number of susceptible infants and children is high due to low vaccination coverage in routine measles programs.

Complacency has clearly been a major obstacle to achieving the goal of measles eradication, together with problems that have arisen as countries put in place new decentralized financial and administrative systems to manage their health systems, including immunization programs. Moreover, there still is a need to disseminate the Plan of Action for Measles Eradication, approved by all Member States in 1995, on a wider scale at the municipal level.

**Table 2. Countries with Measles Outbreaks in the Americas, 1997-1998**

Country	Number of cases		Probable Source of Outbreak
	1997	1998	
Argentina	125	9,469	Brazil
Bolivia	1	1,004	Argentina/Brazil
Brazil	52,284	2,135	Europe
Canada	579	12	Europe/Japan
Chile	58	4	Brazil
Costa Rica	26	20	Brazil
Guadeloupe	116	2	Europe
Paraguay	121	70	Brazil
Peru	95	10	Brazil
United States	138	89	Japan, Europe and Brazil

Another obstacle that needs to be overcome is the lack of national resources to purchase measles vaccines and other supplies in some countries. PAHO has been collaborating with national authorities to ensure that sufficient resources are allocated to maintain adequate stocks of measles and other vaccines, as well as essential supplies. These measures are critical to carry out routine immunization services, for *mop up* vaccination activities, and to quickly implement control measures in the event of an outbreak. An emergency plan was developed for countries in the Southern Cone and Brazil that have been particularly affected by measles outbreaks, to prioritize a public health response in that area. The Minister of Health of Brazil endorsed the Plan, which is already being implemented.

Member States need to take a proactive approach to prevent measles outbreaks. Outbreaks have been opportunities, however, to reinforce surveillance and to obtain the necessary commitment to meet the goal of eradication by the year 2000. Considerably more efforts are needed in analyzing these outbreaks, disseminating lessons-learned among health workers, and in translating this information to decision-makers at the policy level.

It will be critical to implement PAHO's recommended vaccination strategy for measles eradication in full and to include other groups potentially at high-risk for measles, such as health care workers, college and university students and faculty, military personnel and people working in the tourist industry. For measles eradication, annual

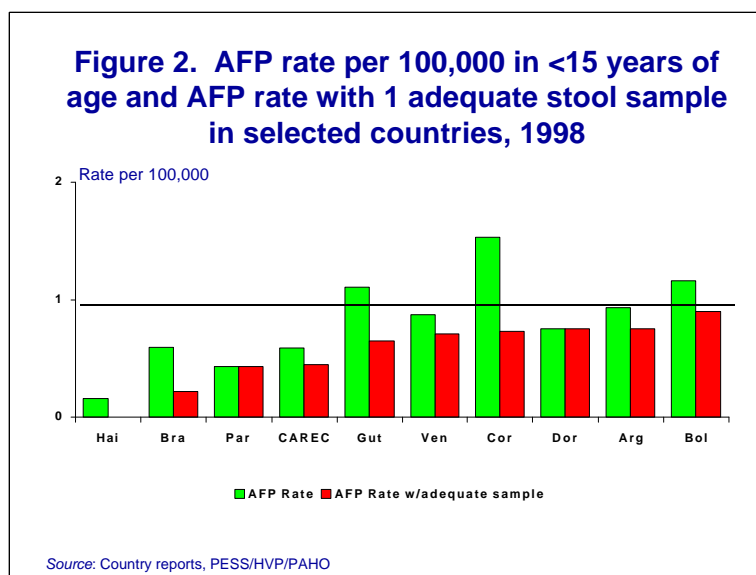


routine vaccination coverage must be at least 95% in every district or municipality of every country of the Region, and follow-up campaigns must be conducted among children 1-4 years of age at least every four years.

As the Region enters the final phase of the measles eradication initiative, a national surveillance system is required that is sensitive enough to detect measles virus circulation in all areas of a country. Sustained efforts are needed to ensure that local surveillance units have the technical, staff, and financial resources to carry out active measles surveillance. The timely detection of a suspected measles outbreak is critical to allow for the rapid implementation of control efforts that will result in decreased transmission. Moreover, the careful investigation of a measles outbreak will provide countries with useful information concerning persons at risk for measles.

### 4.3 Maintenance of Poliomyelitis Eradication

The Region of the Americas has completed its seventh year polio-free. Data coming from the Region continue to show a deterioration in the surveillance of acute flaccid paralysis (AFP) in some countries, especially in the indicators measuring the percentage of cases with one adequate stool sample and that measuring the AFP rate per 100,000 children under 15 years of age, which should be at least 1. The latter is critical because it shows that fewer AFP cases are being detected and entered into the surveillance system, particularly in Haiti, Brazil and Paraguay, as shown in Figure 2. It is imperative that the surveillance system for AFP remains sensitive to promptly detect any reintroduction of the disease in the Region and prevent its spread.



## **5. Sustainable Vaccine Introduction**

The Organization has collaborated with Member States to facilitate the introduction of other vaccines against vaccine-preventable diseases of public health importance. PAHO has supported countries in setting up surveillance systems to monitor the impact of vaccination on the incidence of those diseases in countries that have already introduced additional vaccines and to measure disease burden in those considering future introduction. An objective in forming these surveillance systems is to establish a network of sentinel hospitals in the Region that initially monitors diseases due to *H. influenzae*, and *S. pneumoniae*, and later will include those due to *N. meningitidis*.

Key issues have been the development of a sustainable national infrastructure to accommodate additional vaccines and strategies that countries and the international community should follow to shorten the timeframe from research to the actual widespread and cost effective utilization of vaccines. Given that the price of vaccines remains an important factor, PAHO's Revolving Fund for Vaccine Procurement is playing a mayor role in accelerating the incorporation of additional vaccines, by allowing countries to acquire high quality vaccines at affordable prices.

Particular attention is being paid to including those vaccines that have been on the market for the past 15 years, which include combined measles-mumps-rubella vaccine (MMR) and hepatitis B vaccine, as well as newer vaccines such as *Haemophilus influenzae* type B (Hib) and/or other combination vaccines. In the case of yellow fever vaccine, emphasis has been on stimulating the implementation of an effective vaccination strategy, such as universal vaccination in endemic areas, that will avoid future cases and reduce the possibility of the reurbanization of the disease.

### **5.1 *Haemophilus influenzae* type B (Hib)**

The introduction of *Haemophilus influenzae* type B (Hib) vaccine(s) in the Region represents a useful example of the issues surrounding the sustainable introduction of a vaccine in a national immunization program. By December 1999, PAHO estimates that 81% of all newborns in the Americas (Figure 3) will have Hib vaccine as part of their routine schedule. Considering that the first conjugated vaccines against this pathogen were licensed in the United States, Canada, and Europe only in 1991, their introduction has been remarkably fast and successful.

PAHO has taken a leading role in promoting the establishment of Hib surveillance in the Region and in evaluating the introduction of Hib vaccine in routine immunization programs. These initiatives have been supported by the recommendations of the PAHO

Directing Council and the Meeting of the Technical Advisory Group on Vaccine-Preventable Diseases (TAG). Exchange of experiences among countries at PAHO-sponsored meetings has become an important catalyst to stimulate Hib introduction in routine immunization schedules. The establishment of an epidemiological surveillance network to monitor invasive pneumococcal diseases in children under the age of 5 in six countries of the Region also has had a positive impact on Hib surveillance.

**Figure 3. Hib Vaccine Utilization in the Americas by 1999**



Decisive factors behind the introduction of Hib in several countries include heightened awareness on meningitis diseases among concerned parents; knowledge by the medical profession and health ministries of several clinical trials which point to the vaccine's safety, efficacy and effectiveness; and previous experience with the vaccine in the private sector. Having a well-structured surveillance system that provides the pertinent epidemiological information in advance about the disease is also a critical factor. Countries meeting these requirements have been able to quickly analyze the cost-effectiveness of Hib vaccination and obtain the commitment by government authorities to finance this vaccine on a routine basis.

The existing infrastructure in Chile, Mexico and Uruguay was able to absorb the inclusion of Hib vaccination, without having to incur additional costs for purchasing new equipment for the cold chain, storage and distribution. This situation will vary from country to country based on existing capabilities. The availability of legal support in the form of a presidential decree or a specific vaccine law will foster the continuity and security of the inclusion of other vaccines in the national immunization programs, as has been the case with the introduction of Hib vaccine.

## **5.2 *Rubella and Congenital Rubella Syndrome***

In April 1998, the Caribbean Community announced the goal of eliminating rubella by the year 2000. Between 1992 and 1997, 12 countries reported confirmed cases of rubella. Data from the regional surveillance system established for measles eradication in the English-speaking Caribbean are documenting wide circulation of rubella virus in many countries. In 1996, 672 cases were reported for a subregional incidence rate of 10.3 cases per 100,000 population. In 1997, 603 cases of rubella were reported for an overall subregional incidence rate of 9.2 cases per 100,000 population. In 1998, 47 cases were reported.

Limited surveillance data regarding the prevalence of congenital rubella syndrome (CRS) are available, and most of the experience in CRS surveillance comes from the Caribbean. In 1997 and 1998, a cumulative total of 31 cases of CRS were reported from the Bahamas, Barbados, Belize, Guyana, Jamaica, Suriname, and Trinidad and Tobago. These figures are not accurate due to underreporting. The estimated average cost for rehabilitation and care of an infant with CRS is over US\$ 40,000.

PAHO is working with countries in the Caribbean to develop surveillance case definitions and guidelines that accurately define disease burden. Once the magnitude of rubella and CRS is known and persons at risk are identified, countries can develop appropriate vaccination strategies. During a workshop conducted by PAHO at the Caribbean Epidemiology Center (CAREC) in Trinidad and Tobago in November 1998, there was a review of the methods of rubella/CRS surveillance that have already been implemented by countries of the English-speaking Caribbean. Specific recommendations were made on ways to conduct surveillance throughout the subregion, such as expanding the case classification system to include laboratory and clinically-confirmed cases of rubella, adding several data elements to the case investigation form, including information on pregnancy, and implementing measures to assure adequate laboratory support.

## **5.3 *Yellow Fever***

Although no case of urban yellow fever has been reported in the Region since 1942, more than 1,900 cases of sylvatic (jungle) yellow fever have been reported from Bolivia, Brazil, Colombia, Ecuador, French Guiana, Peru, and Venezuela for the past 10 years. Despite the availability of an effective and safe yellow fever vaccine, low vaccine coverage in many countries means that case and disease outbreaks may continue to occur. So far, the vaccination policy for controlling the disease has been limited to immunizing individuals in affected areas following outbreaks.

The widespread dissemination of the *Aedes aegypti* mosquito throughout the Americas makes the re-urbanization of yellow fever an increasing concern. Member States need to elaborate an effective strategy to control and prevent yellow fever. In order to provide immediate protection to residents in enzootic areas, and to prevent the introduction of yellow fever into nearby urban areas infested with *A. aegypti*, PAHO is recommending that all individuals living in both areas be vaccinated against yellow fever. Coverage of at least 80% is necessary to prevent disease outbreaks in urban areas. The incorporation of yellow fever vaccine into routine childhood immunization programs will be instrumental in achieving high vaccination coverage and in reducing the number of outbreaks. Improved yellow fever surveillance is also critical to effective and timely case identification and for outbreak control response. The Organization has also recommended that a comprehensive vector control program be established by countries to lower the density of *A. aegypti* in urban environments.

## **6. Vaccine Quality and Production**

### **6.1 Vaccine Quality**

PAHO's technical collaboration for quality control of vaccines plays a catalytic role in facilitating and promoting the interaction among eight national control laboratories in Argentina, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico and Venezuela, through their participation in a Regional Network of Vaccine Quality Control Laboratories. These activities are aimed at achieving the harmonization of quality control methodologies in the Region of the Americas and the use of common reference reagents. Some of the laboratories of the Network are providing back-up services for external quality control of vaccine lots. Moreover, a program for certifying laboratories for specific testing is being developed.

Critical for the effective implementation of national immunization programs is the utilization of vaccines of proven quality according to international standards of safety, potency, efficacy and stability. Although the manufacturer is primarily accountable for assuring vaccine quality, this responsibility should also be taken by the national regulatory

authority of the country and shared with managers of national immunization programs. In this regard, PAHO is supporting national regulatory authorities in complying with the basic six functions of: licensing, clinical evaluation, Good Manufacturing Practices inspections, lot release, laboratory testing, and post-marketing surveillance. The Organization is also developing a database for monitoring all vaccine lots released and circulating in the Region.

## **6.2 Vaccine Research, Development, and Production**

The Regional Program of Certification of Vaccine Producers guarantees that vaccines produced in the Region conform to international regulations and Good Manufacturing Practices (GMP). The successful implementation of this certification program requires strong political commitment that will ensure the availability of resources for needed improvements, and the implementation of managerial, administrative and organizational changes that are more in line with productive processes. Such a commitment can be generated if technical and economical feasibility studies are conducted that justify the continuation of production activities. The certification program was initiated with visits to DTP-producing facilities in Chile, in Mexico, and at the Instituto Butantán in Brazil, where vaccine producers are currently implementing the recommendations from expert teams. PAHO is also collaborating with Brazil and Mexico on viability studies of vaccine production in those countries.

Several institutions in the Region have been working independently in the area of conjugated vaccines (*H. influenzae* type b, meningococcal A and C, and pneumococcal vaccines). These institutions need to join forces and collaborate in order to speed up the processes of research, development and production of these conjugated vaccines. In this regard, a meeting on conjugated vaccines held in November with representatives from the vaccine-producing countries of Argentina, Brazil, Chile, Cuba, and Mexico took a step closer to elaborating a strategy for regional technical cooperation towards the development of conjugated vaccines, by strengthening partnerships to work on priority projects.