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VACCINES AND IMMUNIZATION

The following report updates the Executive Committee on the progress towards the goal of measles eradication by the year 2000. It discusses the present epidemiological situation after the re-emergence of the disease in Brazil in 1997 and its subsequent spread to other countries in the Region, as well as the actions undertaken by the countries most affected by measles outbreaks. Detailed discussion centers on measures adopted in the four countries now having major endemic measles transmission. The report commends Member States for their commitment to the measles eradication initiative and urges them to take the necessary steps that will lead the Region of the Americas to successfully achieve this goal. Resources are needed to maintain adequate surveillance and to implement timely "follow-up" measles vaccination campaigns aimed at children 1-4 years of age.

The report notes the significant improvements made in 1999 by most Member States in complying with the four indicators for acute flaccid paralysis (AFP). Those Member States that still need to strengthen AFP surveillance in order to ensure prompt detection of potential disease importations from other regions of the world should act to do so. The steady decline of regional tetanus cases in the Region is highlighted, and recommendations are presented to target vaccination efforts to areas and population groups at highest risk within high-risk municipalities.

Progress by Member States in reaching vaccination coverage levels above 80% is shown. A special call is made to every country to continue developing strategies that will reach population groups still lacking the full benefits of basic vaccination.

An update is given on the remarkable changes taking place in national routine immunization programs in the Americas with the introduction of new vaccines, especially the widespread use of measles/mumps/rubella vaccine and the inclusion of vaccines against *Haemophilus influenzae* type B vaccine, hepatitis B and yellow fever. The report also notes the control strategies being implemented for some of these new target diseases.

The report reviews progress of PAHO's partnership with Member States to ensure that quality vaccines are used in national immunization programs.

The Executive Committee is requested to review the report and make recommendations to the Directing Council on the issues raised.

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1. Vaccination Coverage

Provisional data for 1999 show an increase in vaccination coverage for all antigens in the Americas (Table 1). These figures show that a great majority of children are being immunized through routine vaccination services, but they also point to groups of people within countries still lacking the benefits of basic vaccination. PAHO has called for increased efforts to reach persons living in remote areas, as well as the urban poor who often under-utilize routine immunization services. The challenge ahead is to implement appropriate initiatives which are sensitive to each country's situation in order to effectively reach these groups. Member States should continue monitoring vaccination coverage and disease occurrence by municipality to aid in the development and implementation of a national strategy that effectively reaches unvaccinated children.

Overall regional DPT vaccine coverage in 1999 was 95%; 14 out of 27 reporting countries (52%) had coverage of ≥ 90%. One country reported DPT3 coverage less than 80%: Venezuela (79%).

Overall regional OPV3 vaccine coverage in 1999 was 87%; 14 out of 27 reporting countries (52%) had coverage of ≥ 90%. One country reported OPV3 coverage less than 80%: Ecuador (70%).

Overall regional BCG vaccine coverage in 1999 was 98%; 21 out of 25 reporting countries (84%) had coverage of ≥ 90%.

Overall regional measles vaccine coverage in 1999 was 90%; 20 out of 27 reporting countries (74%) had coverage of ≥ 90%. Countries reporting under 80% are Ecuador (74%) and Venezuela (79%).

2. Measles Eradication

The Region of the Americas is approaching the deadline for indigenous eradication of measles transmission by the end of the year 2000, approved unanimously at the 1994 Pan American Sanitary Conference. Member States are to be commended for their commitment and support to the hemispheric measles eradication goal during the past five years. This support has enabled countries to report significant progress in reducing the burden of measles throughout the Americas. Countries that have followed the vaccination strategy for measles eradication recommended by PAHO are successfully controlling the disease and preventing the occurrence of measles outbreaks.

Table 1. Vaccination coverage of children <1 year of age, Region of the Americas, 1999

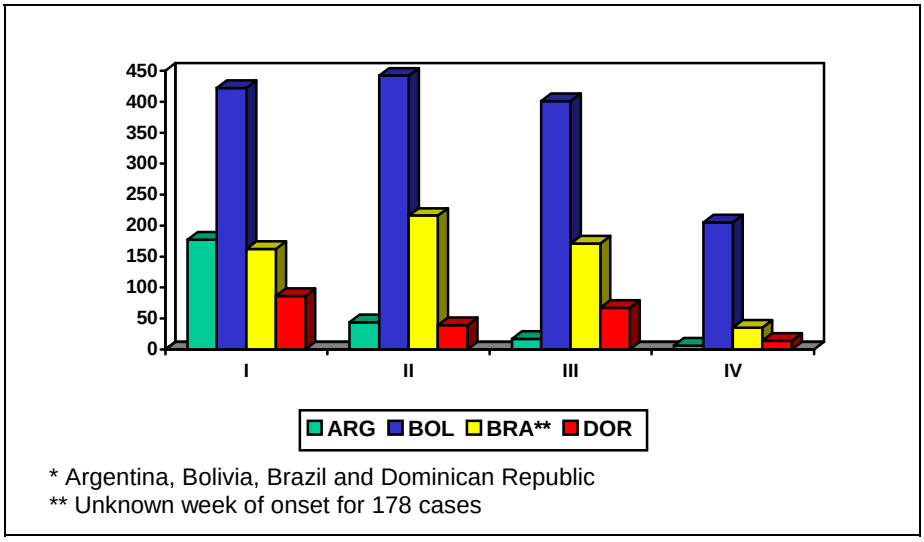
Region/Country	DPT	OPV	Measles	BCG
Andean				
Bolivia	79	73	98	90
Brazil	83	84	90	99
Colombia	...	...	...	...
Ecuador	80	70	74	99
Peru	98	96	92	73
Venezuela	79	82	79	96
Central America				
Belize	87	84	82	96
Costa Rica	93	93	92	83
El Salvador	99	99	98	98
Guatemala	86	86	93	91
Honduras	99	99	99	92
Nicaragua	83	93	97	99
Panama	92	96	90	99
English-speaking Caribbean				
Anguilla	96	99	99	99
Antigua & Barbuda	99	99	99	n/a
Bahamas	...	...	...	...
Barbados	...	...	...	...
British Virgin Islands	90	92	92	99
Cayman Islands	94	94	90	92
Dominica	...	...	...	...
Grenada	88	87	94	n/a
Guyana	83	83	87	91
Jamaica	81	80	82	85
Montserrat	99	99	99	99
St. Christopher & Nevis	99	99	99	99
St. Lucia	89	89	95	99
St. Vincent & Grenadines	...	...	...	...
Suriname	...	...	...	...
Trinidad & Tobago	...	...	...	...
Turks & Caicos	...	...	...	...
Latin Caribbean				
Cuba	94	96	99	99
Dominican Republic	83	84	96	90
Haiti	...	...	...	...
North America				
Bermuda	...	...	...	...
Canada	...	...	...	...
Mexico	96	96	95	99
Southern Cone				
Argentina	...	...	...	...
Chile	89	89	86	86
Paraguay	...	...	...	...
Uruguay	91	85	89	99
TOTAL*	**95**	**87**	**90**	**98**

* Provisional total based on countries reporting as of 17 April 2000
n/a - Data not applicable
... Data not available

During 1999 there were 3,022 confirmed measles cases in the Americas, a decline of 94% from a high of 53,683 cases in 1997. These cases occurred in 11 countries, of which only Argentina, Bolivia, Brazil and the Dominican Republic had indigenous transmission of measles: Bolivia reported 1,445 cases (48% of the Region's total), Brazil 789 (26%), Dominican Republic 2,274 (9%), and Argentina 247 (8%).

PAHO is emphasizing heightened national and international coordination in these priority countries to prevent the spread of measles into other areas. Health authorities in the four priority countries have pledged their full support for the successful conclusion of the regional measles eradication goal. The implementation of a dual strategy of intensive measles vaccination of municipalities that fail to reach ≥ 95 coverage (mop-up), combined with bimonthly active search of measles cases, is being carried out in countries with measles transmission.

Figure 1. Number of confirmed measles cases in priority countries* by quarter, 1999



* Argentina, Bolivia, Brazil and Dominican Republic
** Unknown week of onset for 178 cases

Bolivia was the country most affected by measles, with 48% (1,445 confirmed cases) of all 1999 confirmed cases in the Region, because of large areas with under-immunized populations. The majority of these cases have affected children under five years of age, followed by school-age children (5-19 years) and young adults (20-29 years). Measles virus transmission initially clustered in urban centers and subsequently moved to some rural regions. A Plan of Action was launched by the Ministry of Health to stop the outbreak and interrupt virus transmission. The Plan mobilized technical and financial support from the Government of Bolivia and PAHO, as well as financial assistance from the World Bank, the Inter-American Development Bank,

UNICEF and local non-governmental organizations. The Ministry of Health further issued a Ministerial Resolution supporting the implementation of a comprehensive national vaccination campaign that was carried out in December 1999. For the year 2000, Bolivia has confirmed 37 cases of measles, with the last confirmed case reported on 26 February.

In the Dominican Republic, a measles outbreak began in a tourist area as a result of an importation from Argentina in 1997. Despite two vaccination efforts in 1998, the virus continued to circulate and subsequently spread throughout the country in 1999. Over 50% of the cases were reported from the Santo Domingo metropolitan area, where pockets of unimmunized children, overcrowding in urban areas and low coverage rates from previous *follow-up* campaigns have helped to spread the disease. Similar to outbreaks in Bolivia and other areas in the Region, the majority of cases are found in children under 1 year of age. The country's health authorities and PAHO have organized a task force to ensure the implementation of effective control measures. Active searches for suspected measles cases and *mop-up* vaccination in areas where the virus is circulating are also being conducted. In February 2000, a five–year Plan of Action for immunization developed by the Ministry of Health with PAHO's technical collaboration received funding in the amount of US$13 million from the World Bank, the United States Agency for International Development, the Japanese International Development Agency and PAHO. For the year 2000, no cases have been reported since 18 March.

In Brazil, most states are showing a decrease in transmission thanks to intense surveillance activities by 27 additional epidemiologists hired as part of a special task force formed in 1998. Overall, measles vaccination coverage in 1999 reached 93%, but 59% of the municipalities report coverage under 95%. Through week 13 of 2000, a total of 23 confirmed measles cases have been reported, three with rash onset in 1999 and 20 with rash onset since 1 January 2000. Of these 20 cases, 15 (75%) were reported from six municipalities in the state of Acre. Only 1 confirmed case has been reported since 7 February. Fourteen (93%) of the 15 cases from Acre occurred among unvaccinated persons. The age distribution was as follows: 3 (20%) age <1 year; 5 (33%) age 1-4 years; 4 (27%) age 5-9 years; and 3 (33%) age >20 years. The State of São Paulo reported five cases among vaccinated children age 9-11 months. A *follow-up* measles campaign is scheduled age in some states in June 2000 targeting children 5 to15 years of age.

Progress is also evident in Argentina, which reported the majority of cases in 1998. A provisional total of 789 measles cases were confirmed in 1999, compared to 2,930 confirmed measles cases in 1998. The age group most affected in 1999 was children under 1 year of age, followed by children 1 year of age, and 2-5 year olds. Up to mid-March 2000, four measles cases were confirmed, compared to 113 during the same

period in 1999. An Emergency Plan was developed and four additional national epidemiologists were hired to collaborate with Argentine health authorities in the eradication efforts.

PAHO urges Member States to continue supporting periodic and intensive active search for measles cases, in order to find remaining chains of transmission, particularly in municipalities at high risk for measles outbreaks. At this stage, the implementation of intensive measles vaccination (*mop-up*) of municipalities with disease transmission and in those failing to reach 95% measles vaccination coverage are critical components. Sustained efforts will also be needed to ensure thorough investigation of all outbreaks and the implementation of appropriate public health responses.

3. Diseases

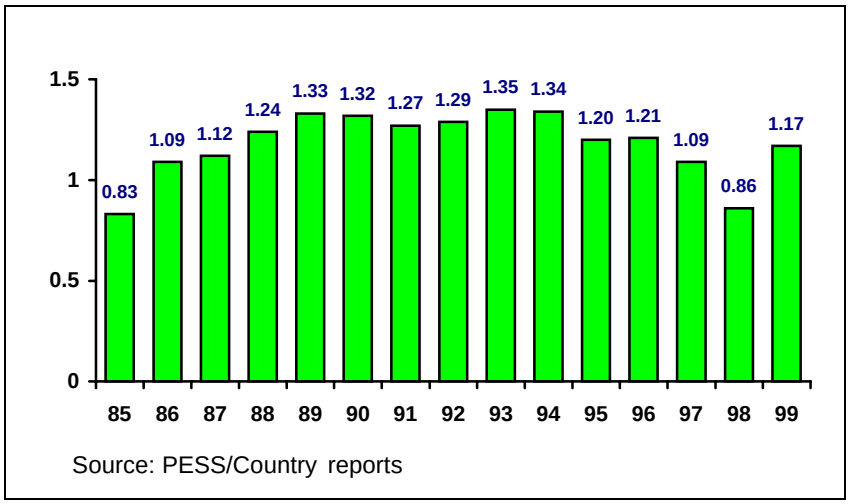
3.1 *Poliomyelitis*

The extraordinary efforts made by all countries worldwide to eradicate poliomyelitis by the end of the year 2000 are bearing fruit, and a polio-free wold is already in sight. At that stage countries in the Americas will join the world in carrying out extensive reviews of surveillance information, which are part of the certification process, to document the absence of circulating wild poliovirus globally. This process will be an opportunity to show that the Region continues to maintain a quality surveillance system, capable of detecting any importation in a timely fashion.

Due to the commendable efforts in several countries, as seen in Figure 2, the indicator of at least one case of acute flaccid paralysis (AFP) per 100,000 for children under 15 years of age shows significant improvement. The latter indicator is critical because it monitors the frequency of AFP cases being detected and entered into the surveillance system. PAHO urges those Member States that still maintain a rate of AFP cases under 1 to take the necessary steps to improve the sensitivity of their surveillance system for AFP.

Maintenance and improvement, where needed, of these surveillance indicators is key for the Americas to retain its certification of eradication status. Member States should also commence a comprehensive inventory of all laboratories, to determine the presence or absence of wild poliovirus, so that the appropriate containment of any virus found can be implemented.

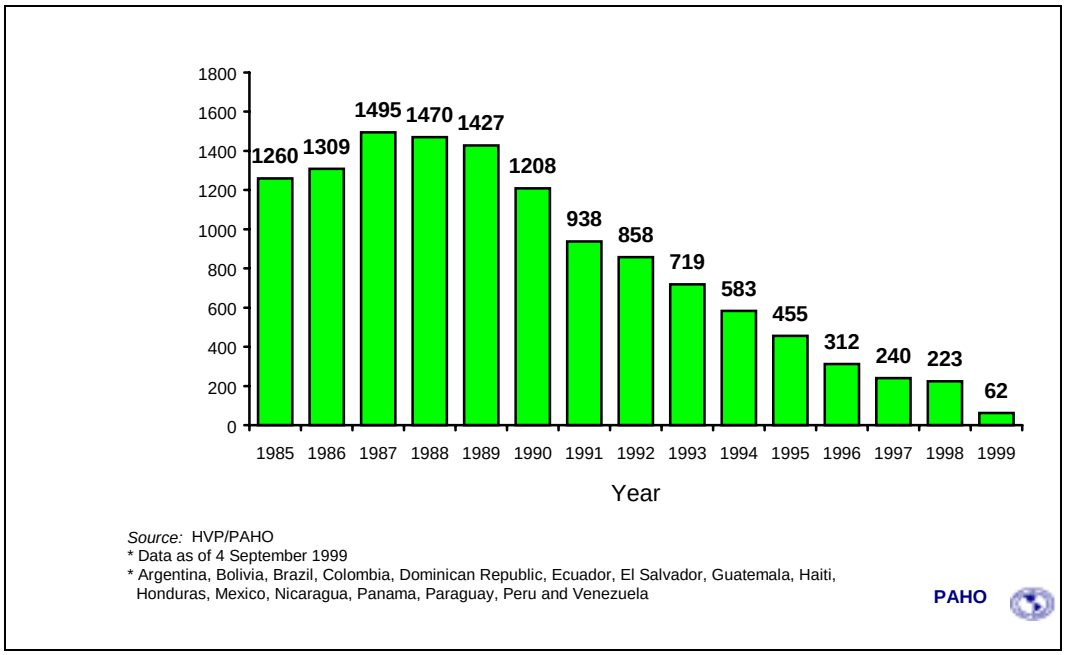
Figure 2. AFP rate per 100,000 children under 15 years of age, Region of the Americas, 1990-1999



3.2 *Neonatal Tetanus*

The total number of cases of neonatal tetanus (NNT) continues to decline as seen in Figure 3. In 1999, the Americas reported 154 cases. The control strategy has been that of vaccinating women of child-bearing age who live in districts classified as high-risk for the disease. Following the notable reduction in cases during the past decade, the 16 countries where NNT is endemic have initiated a new phase of targeting vaccination efforts on areas and population groups at highest risk within those high-risk municipalities that still report isolated NNT cases. For this purpose, PAHO is recommending that countries carry out national evaluations, to determine the number of municipalities remaining in the Attack Phase (intensive vaccination required), and those that have graduated to the Maintenance Phase (vaccination through routine programs). Furthermore, countries should also look into epidemiological and social conditions associated with these remaining cases (migration, lack of vaccination, and marginality, among others), in order to target vaccination toward those groups or areas at greatest risk within high-risk municipalities.

Figure 3. Neonatal tetanus cases per year in selected countries,* 1985-1999



3.3 *Rubella*

In 1999 information obtained on rubella through PAHO's regional measles eradication surveillance system showed that, of 33,633 laboratory analyses performed on samples of suspected measles cases, 8,657 (26%) were confirmed as rubella. Brazil, Dominican Republic, Ecuador, Guatemala, and Nicaragua account for 80% of those cases.

PAHO's cooperation in the control of rubella focused on ensuring widespread rubella vaccination through routine immunization programs, reducing the number of rubella—susceptible women of childbearing age, and supporting countries in the development of integrated surveillance systems for measles and rubella.

Vaccination strategies have already been brought forward to the Member States for either rapidly controlling rubella or for preventing cases of congenital rubella syndrome (CRS). For those countries wishing to rapidly prevent and control CRS, a one-time mass campaign has been recommended, aimed at women between 5-39 years of age, using measles and rubella containing vaccine. Countries wishing to control both rubella and CRS need to conduct a mass campaign for men and women 5-39 years of age with measles and rubella-containing vaccine. The implementation of an integrated measles and

rubella surveillance systems will facilitate the task of Member States in determining the exact location of virus circulation; allow for timely detection of cases to ensure adequate outbreak control and CRS prevention measures; and provide the tools to assess the magnitude of disease burden and the impact of various interventions. A regional standardized surveillance system for rubella and CRS should be developed and implemented.

Chile has carried out a preventive rubella vaccination campaign, targeting women 10-29 years of age to prevent the occurrence of CRS. The campaign achieved 98% vaccination coverage, due in part to the strength of the national immunization program and a highly successful social mobilization campaign. Health authorities have implemented a surveillance system that will provide information on the effectiveness of the campaign and policies, measure its impact on the occurrence of rubella and CRS, and identify groups of people or geographical areas in need of additional control efforts.

Costa Rica also carried out a vaccination campaign following a rubella outbreak in 1999 in which over 250 cases were reported. The measles, mumps and rubella (MMR) vaccination campaign in the country targeted children 1-14 years of age. Selective adult vaccination among risk groups (health workers, educational establishments, tourist workers, and migrants) with MMR vaccine was also carried out. The rubella outbreak in Costa Rica highlighted the need for all countries to adjust their surveillance system for suspected measles cases to include rubella. This outbreak also signaled an increase in rubella activity in almost all Central American countries. Central America countries are moving towards integration of measles and rubella surveillance.

Rubella mass vaccination campaigns have been completed in 5 of the 19 English-speaking Caribbean countries (Bahamas, Dominica, Guyana, Montserrat, and Trinidad and Tobago), achieving vaccination coverage between 67% and 90%. Of the total target population of 2.2 million for all countries, 1,138,454 (52%) have already been vaccinated. *Mop-up* activities are still taking place in those countries. These campaigns have targeted persons up to 40 years of age in some countries, and include males and females. The most frequent age group has been 20-40 years of age, up to 44 years of age in two of the five countries. In 1991 the *catch-up* measles vaccination campaign with MMR vaccine achieved over 90% vaccination coverage in the targeted cohort. This prompted some countries to concentrate on the older age groups.

3.4 *Yellow Fever*

The risk of urbanization of yellow fever in the Americas remains a public health concern, due to the wide and ongoing dissemination of *Aedes aegypti* in the 11 countries located inside the enzootic area (Bolivia, Brazil, Colombia, Ecuador, French Guiana,

Guyana, Panama, Peru, Suriname, Trinidad and Tobago and Venezuela). In 1999, 207 confirmed cases of the selvatic form were reported with 100 deaths, the majority occurring in Brazil, Bolivia and Peru. The growing movement of people from enzootic areas, either by road or air, facilitates the introduction of yellow fever in urban areas, which currently have high rates of infestation with *A. aegypti*.

PAHO is working with Member States to improve epidemiological surveillance and to inform health professionals in high-risk areas of the disease. Bolivia, Brazil and Peru have in place a routine for epidemiological investigations for yellow fever whenever a suspected case is identified. The majority of cases reported in 1999 were laboratory confirmed. So far, only Trinidad and Tobago and French Guiana have introduced a universal vaccination strategy of children. Brazil initiated the implementation of a similar strategy in 17 of its 27 states. Bolivia, Peru and Venezuela are also aiming to introduce yellow fever vaccination in children's basic vaccination schedules by 2000-2001. Vaccination campaigns for other age groups in areas considered at greater risk have also been launched in Bolivia, Brazil, Ecuador, Peru, and Venezuela. Brazil has vaccinated over 35 million people in all age groups in the last two years.

The implementation of strategies to control and prevent yellow fever remain an outstanding issue. PAHO has recommended that all individuals living in enzootic areas and nearby urban areas infested with *A. aegypti* be vaccinated against yellow fever. Coverage of at least 80% is necessary to prevent disease outbreaks in urban areas. The incorporation of widespread yellow fever vaccination in routine childhood immunization programs will be instrumental in achieving high vaccination coverage and in reducing the number of cases and outbreaks in endemic areas. Improved yellow fever surveillance is also critical to effective and timely case identification and outbreak control. The Organization has recommended that a comprehensive vector control program be established by countries to lower the density of *A. aegypti* in urban environments.

4. Quality Control of Vaccines

Key to the success and effectiveness of national immunization programs, besides the availability of adequate infrastructure, logistics and human resources, is the utilization of vaccines of reliable quality. The use of a vaccine of low potency or unknown safety will jeopardize all other efforts and resources invested towards achieving high vaccination coverage. PAHO is, therefore, placing high priority on establishing and strengthening the mechanisms that will allow countries to guarantee the utilization of quality vaccines.

Efforts have been directed towards strengthening the national regulatory authorities in the Region to ensure compliance with the six regulatory functions of:

(a) licensing of all vaccines used in the country; (b) clinical evaluations of vaccines; (c) release of every vaccine lot to be used in the country; (d) access to a laboratory that can perform vaccine testing; (e) inspections of manufacturers to evaluate compliance of Good Manufacturing Practices; and (f) the implementation of a post-marketing surveillance system.

In the area of national regulatory authorities, the Organization collaborated with Member States in the harmonization of regulatory activities for the licensing of vaccines in non-producing countries, particularly in the Central American countries and in the Dominican Republic. A generic document with harmonized procedures for vaccine licensing was developed and is currently in use in several countries. In order to strengthen the regulatory functions in these countries, workshops were developed and carried out on topics surrounding the process of vaccine licensing, lot release, and Good Manufacturing Practices (GMP). Computers and access to Internet were provided to improve communication and to implement the database systems for registering circulating vaccine lots.

Efforts in the area of quality control were also directed toward assisting the national control laboratories of Argentina, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico, and Venezuela in achieving levels of proficiency and qualification. This task seeks to standardize laboratory methodologies, production and distribution of reference reagents, training on control of new vaccines, validation of alternative *in vitro* potency tests, and improvement in communication and exchange of information among participating laboratories. A certification program to assess the proficiency and performance of laboratories in the regional network was developed and implemented in order to guarantee access to vaccine testing at qualified laboratories, either by PAHO or by a national regulatory authority in the Region. A database developed for the registration of all vaccine lots released and circulating in the Region was improved and is currently being evaluated by selected national regulatory authorities and laboratories.

Several countries in the Region are currently manufacturing some of the vaccines used in regular immunization programs, while others are seeking to initiate local production. This underscores the need that current and prospective producers comply with international requirements and GMP. PAHO has previously emphasized the importance of strong political commitment to ensure the availability of resources that will enable producers to carry out improvements of existing facilities, as well as changes in managerial, administrative and organizational areas. The Organization continues to promote technical and economic feasibility studies of vaccine producers in the Region, which once conducted will provide information that can justify the continuation or termination of production activities. Mexico carried out such as study, and Brazil has

requested assistance to perform a similar study. Peru has also expressed interest as it is considering local production of yellow fever vaccine. Recommendations on carrying out these studies have been provided to Colombia, Ecuador, and Venezuela.

The Organization is also collaborating with WHO in promoting the inclusion of local vaccine manufacturers in WHO's assessment process. If passed, vaccine producers in the Americas could become vaccine suppliers to United Nations agencies. Cuba has initiated this process for hepatitis B vaccine, and Biomanguinhos of Brazil, for yellow fever vaccine. PAHO is also providing technical advice to the recently formed Global Alliance on Vaccines and Immunization (GAVI), especially to its research and development pre-task force. Initial steps have been those of developing an inventory of pilot lots and contacting manufacturing facilities in the Region to locate potential facilities that could be useful in the various stages of development of "orphan" vaccines of public health importance.