

Protecting the Health of the Americas: Moving from Child to Family Immunization



FINAL
REPORT

**XVII Meeting of the Technical Advisory Group
on Vaccine-preventable Diseases
Guatemala City, Guatemala - 25-27 July 2006**



Immunization Unit
Family and Community Health Area



**Pan American
Health
Organization**

Regional Office of the
World Health Organization

TECHNICAL ADVISORY GROUP ON VACCINE-PREVENTABLE DISEASES

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PROTECTING THE HEALTH OF THE AMERICAS: MOVING FROM CHILD TO FAMILY IMMUNIZATION

The XVII Meeting of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases of the Pan American Health Organization (PAHO) was held from 25-27 July 2006 in Guatemala City, Guatemala. The TAG recognized the substantial progress achieved by member countries since the last meeting in 2004, and the high quality presentations and abstracts at this meeting. This meeting focused on the new challenges involving the transition from child to family immunization. In addressing this unfinished agenda –protecting achievements and facing new challenges– representatives from countries of the Region of the Americas shared their experiences since the last TAG.

While polio was eradicated in the Region over 15 years ago (Figure 1), indigenous measles transmission eliminated in November 2002 (Figure 2), and neonatal tetanus eliminated in all but one of the countries of the Region (Figure 3), challenges remain with other vaccine-preventable diseases threatening vulnerable populations. The effort continues to maintain measles eradication and to eliminate rubella and congenital rubella syndrome, as well as with initiatives to introduce new and underutilized vaccines (influenza, yellow fever, rotavirus, pneumococcal conjugate, and human papillomavirus) and to implement enhanced surveillance techniques, vaccine safety assurance, and data management.

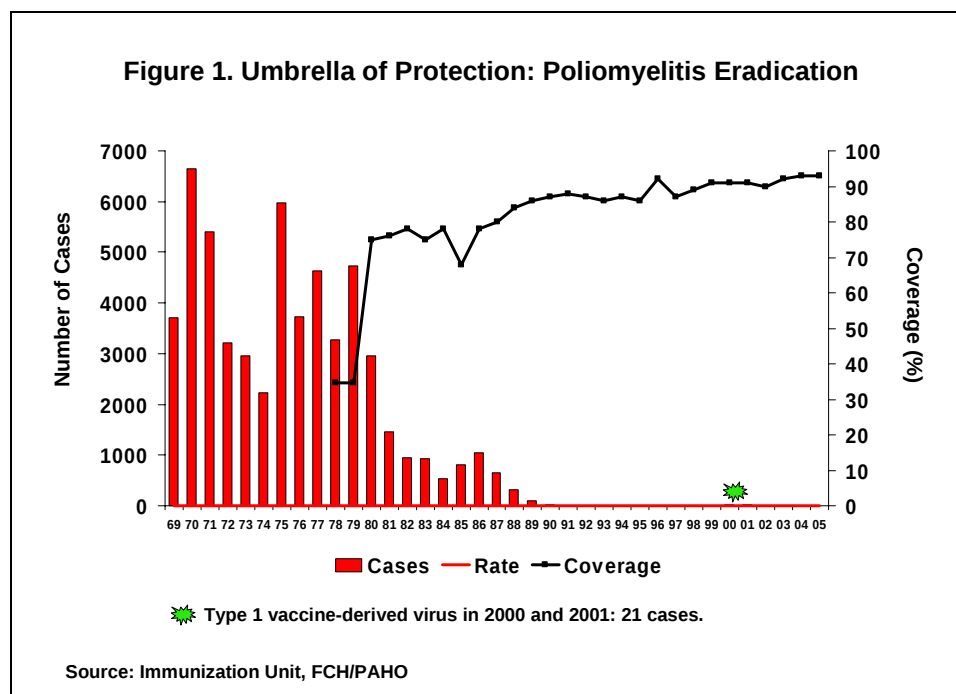
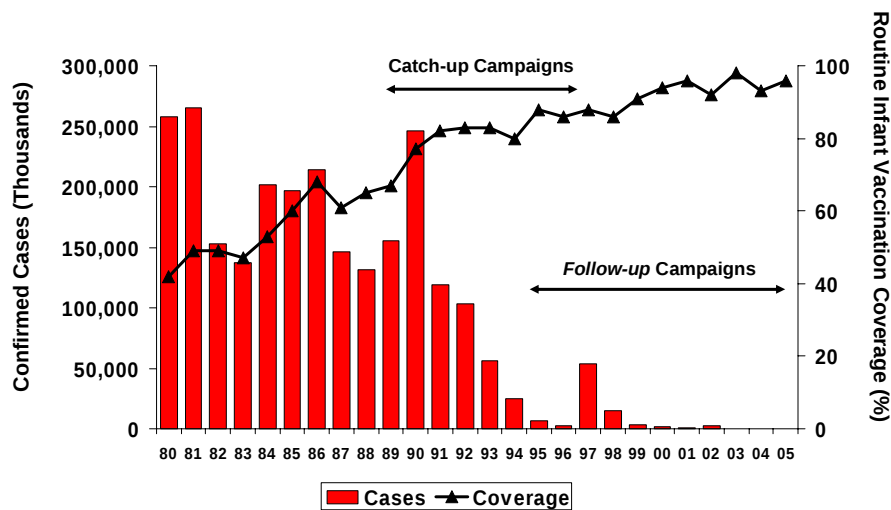


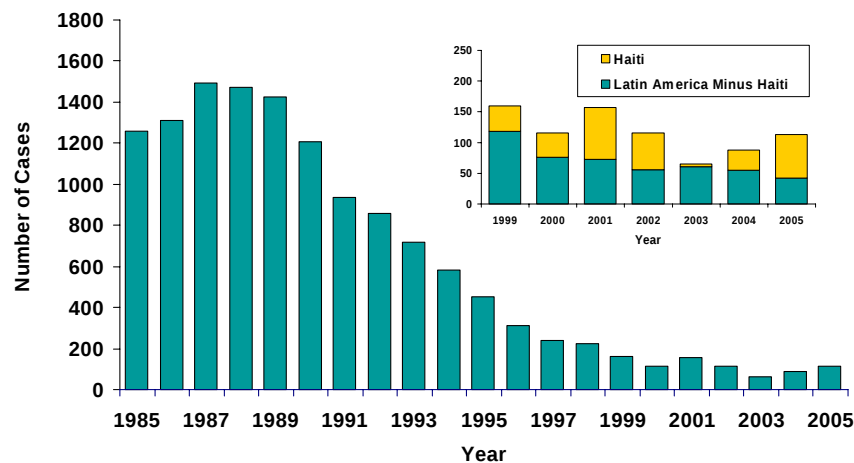
Figure 2. Umbrella of Protection: Measles Elimination



Source: Immunization Unit, FCH/PAHO

Note: 81 confirmed cases in 2005.

Figure 3. Umbrella of Protection: Neonatal Tetanus Elimination



Countries with cases in the last 3 years: Argentina, Bolivia, Brazil, Colombia, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, and Venezuela

Source: Country reports.

Immunization is one of the most cost-effective interventions available in public health. Countries should therefore be prepared to face challenges ahead that will be even more daunting with the advent of so many new vaccines in the 21st century, which will be known as the “Century of vaccines”. The Expanded Program on Immunization (EPI) makes a significant contribution towards achieving the Millennium Development Goals of reducing child mortality and improving maternal health, and is a key tool for the promotion of socioeconomic development.

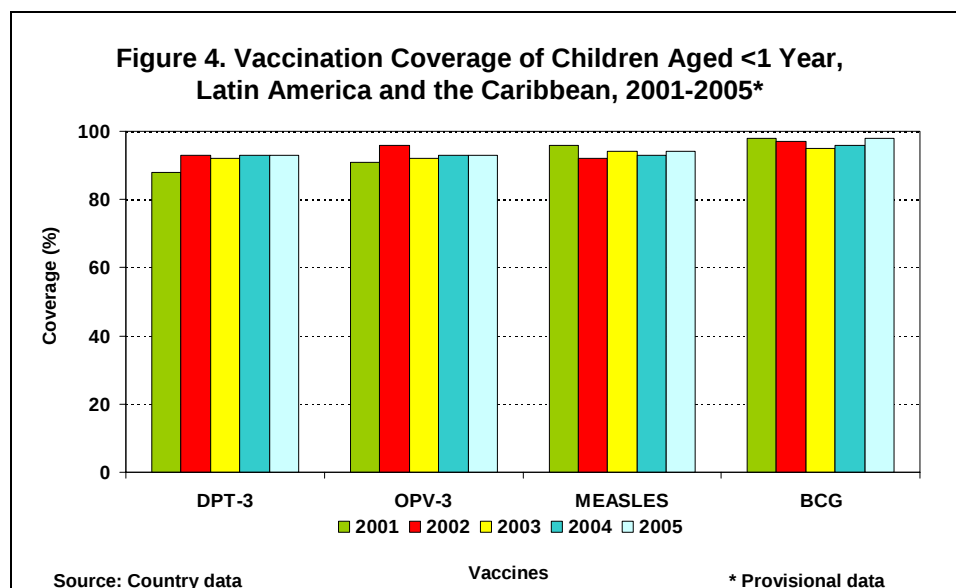
Dr. Ciro de Quadros, Chairman of the TAG, opened the meeting. He was followed by Dr. Rudy Eggers, World Health Organization (WHO), Geneva, who reiterated the call for action on rubella elimination. Dr. Mercy Ahun presented on behalf of the Global Alliance for Vaccines and Immunization (GAVI), highlighting the need to continue to support the world's poorest countries. Dr. Gina Tambini, Manager, Family and Community Health Area, PAHO, provided participants with an update on the status of the follow-up of recommendations of the 2004 TAG meeting in Mexico City. Representatives from partner organizations such as the US Centers for Disease Control and Prevention (CDC), GAVI, PATH, Sabin Vaccine Institute, and UNICEF made statements of support to immunization programs in the Region. Dr. Joxel García, Deputy Director, PAHO, and Dr. Marco Tulio Sosa, Minister of Health of Guatemala, officially opened the meeting by making remarks stressing the importance of achieving and sustaining Regional initiatives such as measles and rubella elimination. Dr. Jon Kim Andrus and Dr. Tambini served as *ad-hoc* Co-Secretaries of the meeting.

TAG members were pleased to note that PAHO continues to provide leadership in addressing the critical issues of inequities in health, strengthening public health infrastructure, promoting a culture of prevention, galvanizing political commitment, and promoting excellence in technical cooperation, and that its Immunization Unit continues to serve countries as a Regional Program supported by:

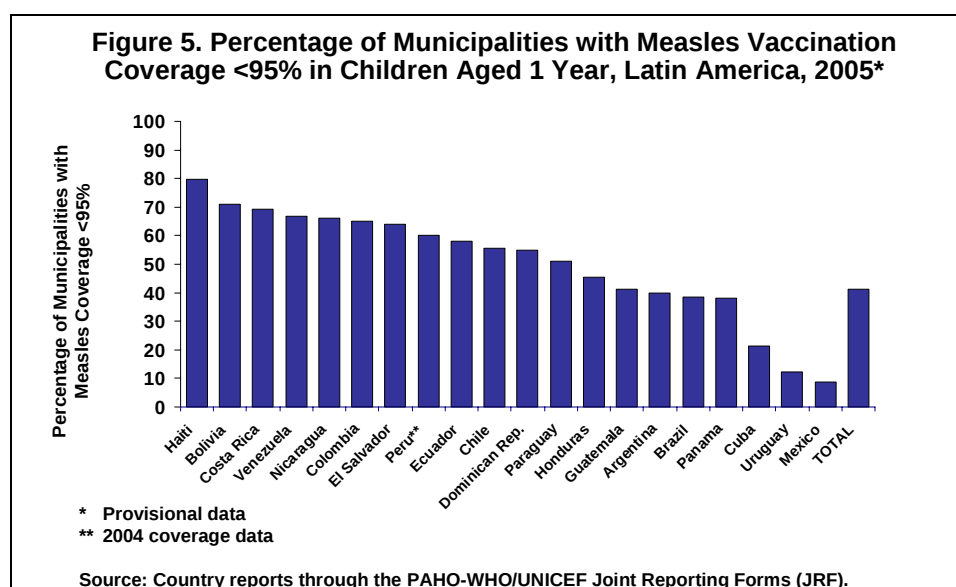
- A regional interagency coordinating committee to review and galvanize funds for resource gaps, which recognizes PAHO as the technical secretariat;
- Subregional meetings of EPI managers;
- Standard goals and targets for improving immunization coverage and surveillance of vaccine-preventable diseases;
- National plans of action with clear objectives to implement and execute the strategies to reach the goals;
- Capacity development of institutions and personnel; and
- A technical advisory group that meets regularly to review program progress.

ROUTINE IMMUNIZATION

Routine coverage for BCG, DTP-3, and Polio-3 in children aged <1 year and measles-containing vaccines in children aged 1 year remains over 90% at the Regional level (Figure 4). Also, as of 2006, all countries in the Region but Haiti are using MMR vaccine and have introduced vaccines against *Haemophilus influenzae* type b (Hib) and hepatitis B, with 31 countries using the pentavalent¹ vaccine.



While the reported coverage at national level is high throughout the Region, heterogeneity in coverage exists at municipal level, with a significant proportion of municipalities reporting coverage <95% (Figure 5).



¹ Pentavalent vaccine refers to the combination DTP-Hib-Hepatitis B.

Given that equity is a key principle of PAHO's technical cooperation, national immunization programs, with PAHO support, should continue to focus on increasing resources and developing strategies to reach every child and family in these low-performing municipalities.

Recommendation:

- TAG reaffirms the recommendation that all countries should achieve $\geq 95\%$ vaccination coverage with all antigens in every municipality.

RUBELLA AND CONGENITAL RUBELLA SYNDROME

Rubella is a self-limited febrile rash illness with few complications. However, if a woman contracts the infection in the early stages of her pregnancy, the rubella virus has devastating consequences and may cause a syndrome known as congenital rubella syndrome (CRS). The high probability of fetal infection (90% if the infection occurs before the 11th week of gestation) and the severity of its manifestations, among them miscarriage, stillbirth, mental retardation, and serious birth defects such as deafness, blindness, and congenital cardiopathy, highlight the importance of implementing effective strategies for prevention of this disease. It has been estimated that, before vaccine introduction into national immunization schedules, more than 20,000 children were born with CRS each year in the Region.

In 2003, the PAHO's Directing Council adopted Resolution CD44.R1, calling for rubella and CRS elimination in the Americas by the year 2010. Rubella elimination has been defined as the interruption of endemic rubella virus transmission in all countries and the lack of indigenously acquired CRS cases. Since humans are the only host of the rubella virus and a very effective vaccine (>95% efficacy) conferring lifelong immunity is available at a low cost, elimination is achievable. It will become the second greatest achievement of immunization in the Americas in the 21st century, following the interruption of endemic measles transmission in 2002.

In their efforts to achieve elimination, countries should conduct a one-time mass campaign, vaccinating both men and women with MR or MMR² vaccine. To ensure the implementation of the highest quality campaigns, the following criteria should be fulfilled:

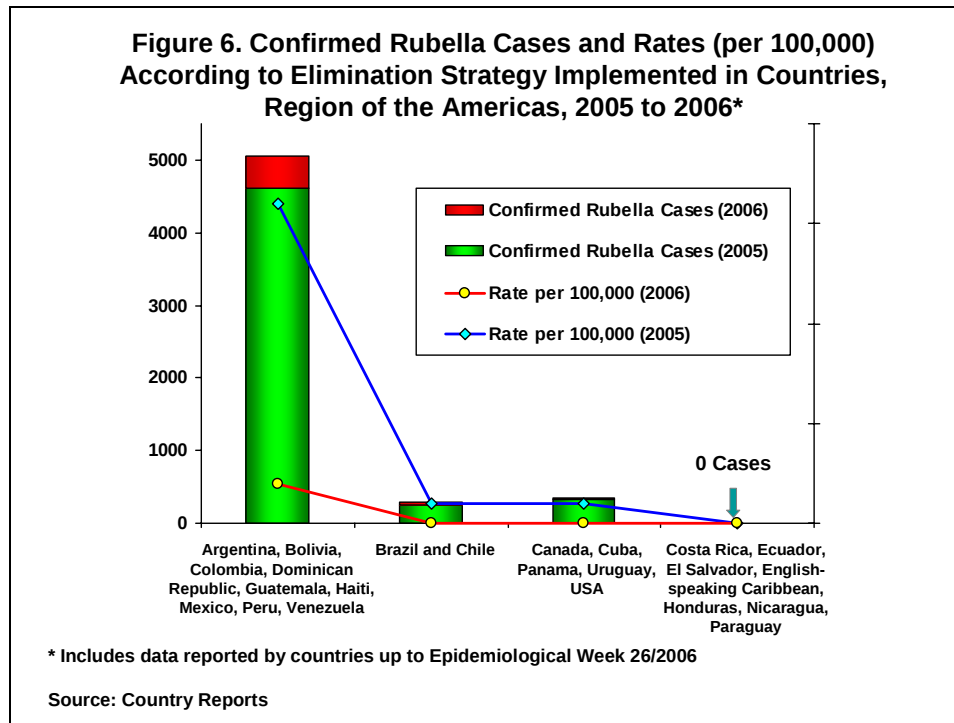
- The age group to be vaccinated should be determined based on the epidemiology of rubella in the country, an assessment of the susceptible population, the year of vaccine introduction, subsequent rubella vaccination campaigns, and the need to protect women of childbearing age (WCBAs).
- Quality campaigns require vaccinating both females and males, including susceptible adults, and reaching coverage levels close to 100% of the targeted population.
- The highest political commitment and participation should be ensured.
- Full population participation requires intensive social mobilization and local micro-planning.
- Information system should be practical and useful.
- Capacity to detect and rapidly respond to safety concerns and other emerging issues during campaigns.

The implementation of a one-time, high-quality mass vaccination campaigns in both men and women has proven to be effective in the Americas and countries that did so have interrupted transmission. Countries that still have a pool of susceptibles by not vaccinating both men and women (i.e., targeting women only), are continuing to have a low level of endemic transmission of the rubella virus, and are potentially putting other countries of the Region at risk.

By June 2006, 37 (80%) of the countries and territories of the Americas had implemented vaccination campaigns (accounting for 75% of the population of the Region), obtaining coverages of over 95%. The seven remaining countries are expected to complete their campaigns by June 2007.

² Safety and supply/cost concerns should be considered when using MMR.

Regional progress toward elimination of rubella has been remarkable. The number of confirmed rubella cases decreased by 96.2% between 1998 and 2005 (from 135,947 to 5,209).³ The impact has been greater in countries that vaccinated men and women (0 rubella cases, after the campaigns) compared with countries where only women were vaccinated (N = 254, rate = 0.1 per 100,000). Rubella incidence was greater in the group of countries that have not yet implemented vaccination campaigns (N = 4,618, rate = 1.6 per 100,000) (Figure 6).



Comprehensive surveillance of measles and rubella has been strengthened. By epidemiologic week 26 of 2006, 97% of suspect cases had been discarded following laboratory testing. Prior to implementing the elimination strategy, less than 20% of rubella cases were confirmed by laboratory or epidemiological link; this figure rose to 96% in 2005.

The seven surveillance indicators endorsed by the 2004 TAG are as follows: the percentage of sites reporting weekly, the percentage of suspect cases with adequate epidemiological investigation, the percentage of cases with adequate blood sample, the percentage of samples received by the laboratory ≤ 5 days, the percentage of laboratory results reported ≤ 4 days, the percentage of cases discarded by laboratory, and the number of chains of transmission with representative samples for viral isolation. Overall, performance for three of these indicators is weak. Up to week 26 of 2006, the percentage of cases with adequate investigation was only 78%, only 56% of samples reached the laboratory within 5 days, and only 69% of laboratory results were reported within 4 days. Furthermore, very few samples for virus isolation have been collected to date.

The best public health practices are being identified to improve CRS surveillance at the primary care level, strengthen the capacity to diagnose deficiencies in health services, and ensure expert review of suspect CRS cases. The goal of CRS surveillance is to monitor trends, help identify

³ Provisional data as Epidemiological Week 28, 2006.

reservoirs of transmission, and to serve as a critical advocacy tool. In 2005, 1,952 suspect CRS cases were reported and 20 were confirmed.³ By epidemiological week 26 of 2006, 342 suspect CRS cases had been reported and one was confirmed.

Advances have been made in the development of laboratory capacity to detect and isolate rubella viruses, increasing knowledge of the endemic genotypes in the Region. The most frequent genotype is 1C, followed by 1E, and 1g. The last two genotypes were linked to imported cases in epidemiologic investigations. However, the number of specimens for rubella virus isolation is still limited (in 2005, only 93 specimens were collected for isolation) and should be substantially increased to better document endemic virus reservoirs and imported virus genotypes.

TAG is concerned that insufficient laboratory results are being reported within 4 days of receipt of the sample at the laboratory. In some countries, the timeliness of this indicator is being affected by the number of subnational laboratories that do not receive enough samples to process them immediately. These laboratories wait to accumulate samples before processing them in order to avoid wasting their kits. In other countries, the indicator is being affected by the delayed entry of the laboratory result into the national database.

Recommendations:

TAG congratulates member countries for the significant progress made toward the goal of rubella and CRS elimination by 2010. Given the countries' successes, the goal is certainly achievable for the Americas.

Vaccination Strategies

- In accordance with previous TAG recommendations, all endemic countries are encouraged to implement a one-time mass vaccination campaign targeting both men and women and achieving $\geq 95\%$ coverage.
- TAG recommends that the criteria for high quality campaigns outlined above be included in the design and implementation of rubella mass vaccination campaigns. Those countries that did not vaccinate all susceptibles in the population should analyze their data, in particular to identify the susceptible male population (in which sustained transmission can occur) that should be vaccinated. PAHO should provide support in this process.
- TAG encourages countries to document the experiences, successes, and lessons learned from their adult mass campaigns in order to share them with other countries. These lessons will be useful for the introduction of HPV vaccine and eventually a vaccine against HIV/AIDS.

Surveillance

- Full integration of measles and rubella surveillance is required; integrated laboratories are an important aspect of this surveillance system. Emphasis must be placed on active surveillance. Except in outbreak settings, all specimens must be tested for both measles and rubella.
- Countries should ensure that the seven indicators meet the recommended standards. Special attention should be given to checking clusters of suspect cases as well as "silent areas".

- Countries should review and improve the quality of their surveillance and information systems with PAHO support, as needed.
- TAG endorses the following recommendations reached through consensus by the participants of the *Ad-hoc* meeting of experts on “best practices in CRS surveillance”:
 - Sensitivity and quality of surveillance system should be increased by strengthening sentinel site reporting – including secondary and tertiary hospitals, specialty clinics, and the use of TORCHS⁴ for differential diagnosis as part of CRS surveillance;
 - The use of information should be strengthened, such as the information generated by the perinatal information systems of CLAP⁵ and ECLAMC⁶ and national databases related to child and maternal health, in order to increase the capability for CRS case detection.
 - Strong partnerships should be built with professional and academic institutions and societies in order to train professionals and involve them in rubella and CRS surveillance efforts. The modules and field guides published by PAHO should be disseminated with this objective in mind.
 - A multidisciplinary team should be formed in each country at national level, similar to the one used for polio eradication, to evaluate and classify suspect cases.

Laboratory

- The number of clinical specimens collected for viral isolation should be increased in order to document the endemic genotypes of rubella and the interruption of endemic transmission of rubella in the Americas.
- In a pregnant woman, IgM should be obtained only when there is a history of rash or contact with a rubella-like rash. IgM is NOT recommended for routine antenatal testing.
- The serological and virological laboratory testing of all suspected CRS cases should be encouraged.
- TAG recommends that PAHO review the laboratory network, with special attention to the subnational networks, to identify the possible bottlenecks and propose corrective actions.

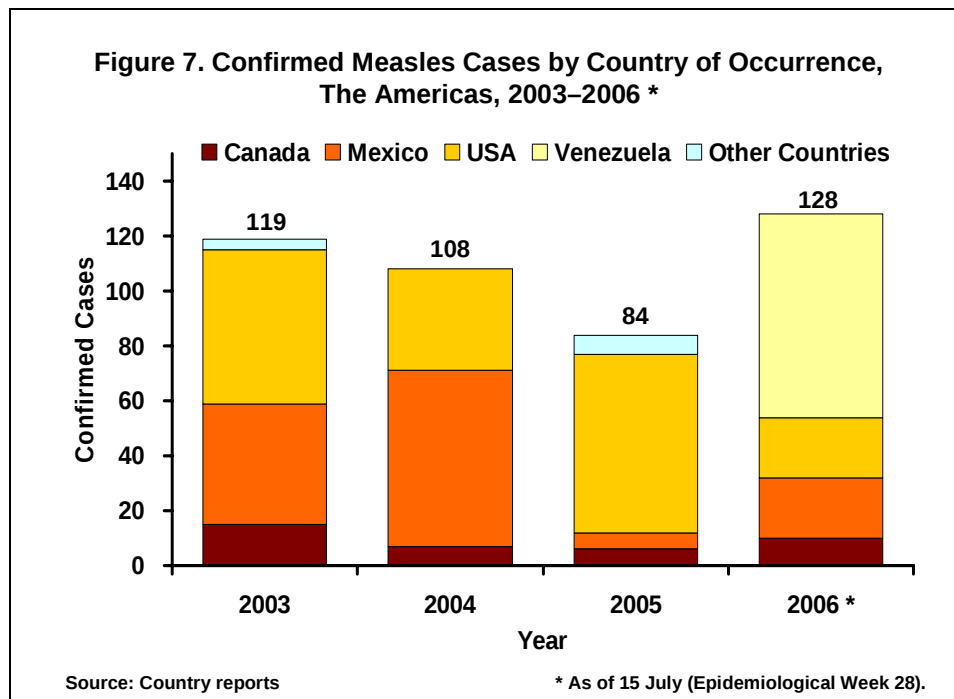
⁴ TORCHS stands for Toxoplasma gondii; other viruses (HIV and more); rubella (German measles); cytomegalovirus; herpes simplex; and syphilis.

⁵ CLAP: Spanish acronym for the Latin American Center for Perinatology and Women and Reproductive Health.

⁶ ECLAMC: Spanish acronym for the Latin American Collaborative Study on Congenital Malformations.

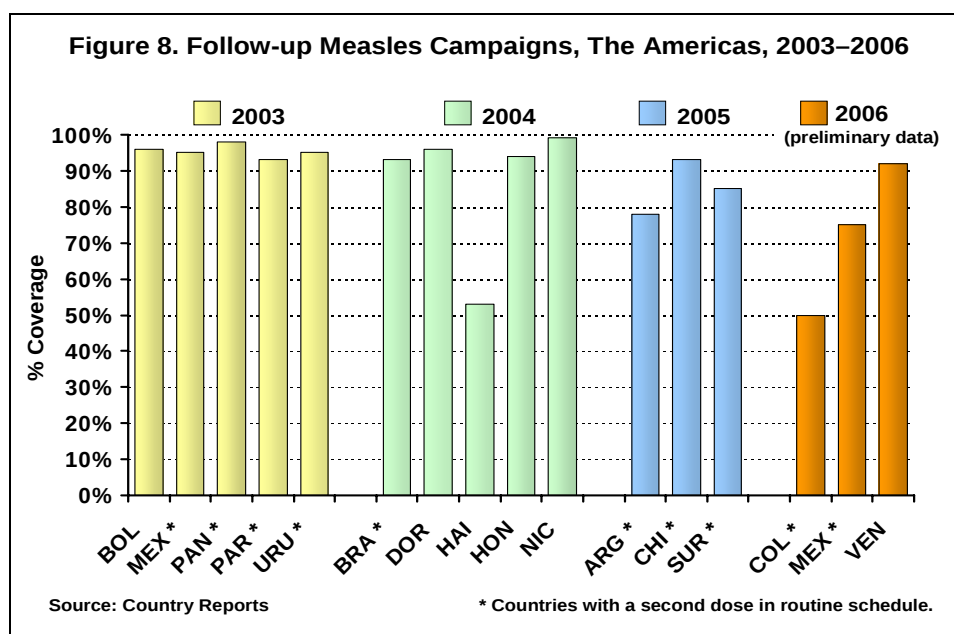
MEASLES

Absence of widespread measles virus transmission since November 2002 is proof of the success of the measles elimination initiative in the Americas. However, the endemic measles virus circulation in other parts of the world puts our Region under constant threat of importations. Fifty-one percent of the 370 measles cases reported in the Americas between January 2003 and April 2006 were positively linked to an importation. Importations occurred from all other WHO Regions. Six outbreaks with >10 cases were detected since 2003 (range = 10–108 cases) (Figure 7).



Countries must avoid becoming complacent to the risk of measles importation and the potential for reestablishment of endemic measles transmission. Occurrence of measles cases among children aged 1–4 years in outbreaks in Mexico and Venezuela indicates a weakening of routine vaccination. National *follow-up* campaigns that should have been conducted every 3 to 4 years have either been cancelled or postponed indefinitely in some countries. Finally, indicators of integrated measles/rubella surveillance have not shown improvement or have worsened.

As areas of great inequity remain throughout the Americas, reestablishment of endemic measles virus circulation upon importation remains a distinct possibility and would undermine significant progress in reducing child mortality. While coverage with measles-containing vaccine at regional level was 93% in 2004, 42% of municipalities had coverage below 95%— an indication that coverage remains uneven and that significant pockets of susceptible groups exist in our Region (Figure 8). The decision by some countries in Latin America and the Caribbean to move away from *follow-up* campaigns and towards a second routine dose raises concerns that many marginalized and hard-to-reach children may never have an opportunity to be vaccinated against measles and represents a risk for the occurrence of large outbreaks.



Recommendations:

TAG recognizes the important efforts that countries have made towards maintaining measles eliminated in the Americas. In order to ensure its long-term sustainability in the absence of a global measles eradication goal, the following recommendations are made:

- Countries should identify municipalities with less than 95% coverage for measles-containing vaccine and devise strategies to reach and maintain coverage in the 95%–100% range in every municipality.
- High-quality nationwide *follow-up* campaigns (achieving coverage $\geq 95\%$ in every municipality) should be conducted every 3 to 4 years (earlier if a susceptible accumulation above 80% of a typical birth cohort has accumulated), irrespective of whether a second MMR dose is included in the national routine immunization schedule. Only where coverage $\geq 95\%$ with each of the two MMR doses is guaranteed for all municipalities can the *follow-up* campaigns considered to be waived.
- The Vaccination Week in the Americas, targeting low-coverage municipalities and under-served or hard-to-reach population groups, present an excellent opportunity to reach unvaccinated children.
- Vaccination of at-risk professional groups, such as workers in the health care, transportation, and tourism sectors, is recommended and should be verified regularly through an established formal process.
- Any resident of the Americas traveling to areas with reported measles (or rubella) cases should be immune to measles (and rubella) before departure. Requesting proof of vaccination from incoming travelers is not advised.

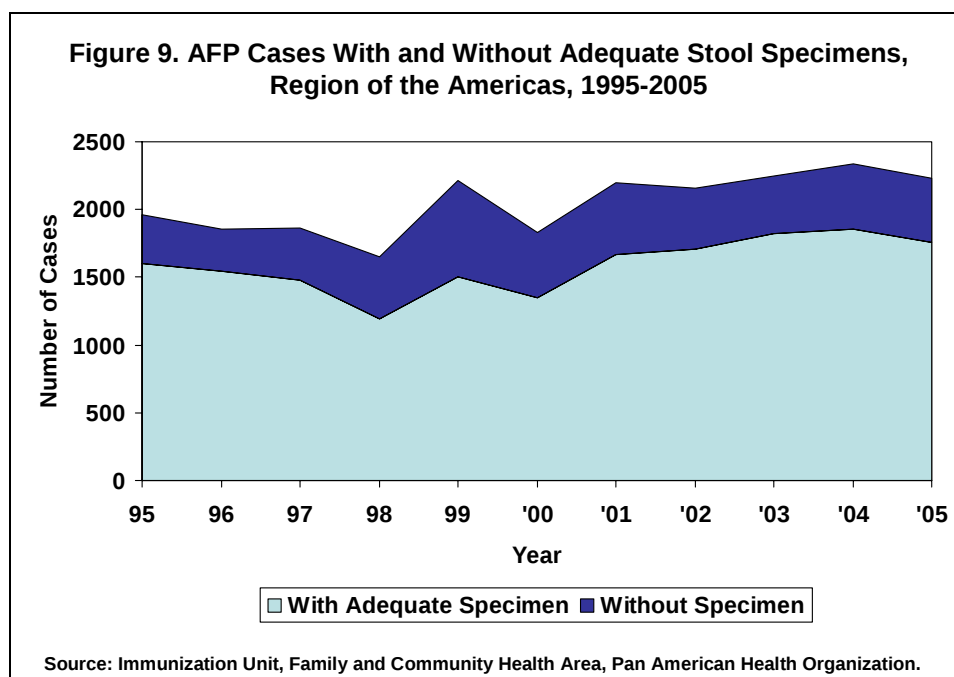
- Integrated surveillance for measles/rubella should include private institutions, including those attended by tourists, to increase sensitivity and timely detection of imported cases.
- All indicators of measles/rubella surveillance need to be met and constantly monitored to ensure compliance when necessary and guarantee the quality and sensitivity of surveillance. In order to protect the Region against the consequences of importation, it is imperative that countries ensure measles coverage $\geq 95\%$ in all municipalities and very sensitive and high-quality surveillance data.
- The final report and recommendations of the Measles/Rubella Laboratory Network Meeting are endorsed by TAG.

During the measles session of the meeting, Uruguay presented data on an ongoing extensive mumps outbreak. Given that data on this outbreak revealed new age groups at risk for mumps infections, TAG recommends PAHO conduct a regional assessment of the epidemiology of mumps in the Americas to be presented at the next TAG.

POLIOMYELITIS

The Western Hemisphere was certified as free of the circulation of the indigenous wild poliovirus in 1994 and the last case of poliomyelitis caused by a wild poliovirus was detected in Peru in 1991.

Acute flaccid paralysis (AFP) surveillance remains in place in the American Region. The AFP rate continues above 1/100,000 children aged <15 years and the proportion of adequate specimens remains at approximately 80%. The level of compliance with the last indicator underscores the need for an independent body to help every country with classifying the remaining 20% of cases (around 400–500 cases per year) without adequate specimens (Figure 9).



The feasibility of global polio eradication in the near future was reaffirmed in Geneva, in 2005, by the Advisory Committee on Polio Eradication (ACPE) and at the World Health Assembly in May 2006. Indigenous polio transmission is still occurring in Nigeria, India, Pakistan, and Afghanistan, while several other countries previously free of polio have been recently re-infected. These include some African countries, such as Angola, which have close ties with the Americas. Therefore, after fifteen years of being free of wild polioviruses, the American Region remains at constant risk of polio importations from countries where wild poliovirus still circulates widely. The number of polio cases worldwide was 1,255 in 2004, and 1,951 in 2005.

The vaccine-derived outbreak of polio in 2000-2001 in the Dominican Republic and Haiti highlights the risk of low OPV coverage in countries and municipalities, and the risk of failing to timely detect the circulation of poliovirus. TAG supports the need to minimize the potential for reintroduction of wild poliovirus through containment of poliovirus strains in the laboratories. Seven countries out of 44 countries and territories have already completed Phase 1 of containment. While some progress has been made, countries should make every effort to conclude phase I of containment before the end of 2006.

Recommendations:

- OPV remains the vaccine of choice in the final phase of global polio eradication.
- To reduce the risk of importations and to prevent another outbreak caused by a Sabin-derived poliovirus, countries that do not achieve OPV coverage $\geq 95\%$ in every municipality must conduct annual OPV immunization campaigns for children aged <5 five years, regardless of their vaccination status.
- Countries must maintain high quality AFP surveillance, strengthen the polio laboratory network, and complete phase I of laboratory containment of wild poliovirus by the end of 2006. PAHO should establish a panel of experts to review country reports on laboratory containment and provide feedback to the countries. All countries in the Region must maintain high polio vaccination coverage of at least 95% of children aged <5 years in every municipality.
- Countries should establish a national expert group or commission that closely scrutinizes the compatible polio cases without adequate stool specimens. Every one of those cases must have a written report specifying the final classification and the criteria used by the expert group to determine that classification.

LABORATORY NETWORKS

Measles/Rubella Laboratory Network

The Measles/Rubella Laboratory Network continues to be fully functional and supports the surveillance of measles/rubella in the Region. The network has provided crucial information in order to confirm or discard suspect cases, identify virus strains circulating in the Region, and evaluate the impact of mass campaigns activities that are critical for the surveillance.

Laboratory investigations are enhanced by the use of standardized diagnostic methods and reagents, and by implementing a quality assessment program, including an annual accreditation review, proficiency testing, and reporting of laboratory indicators. Although considerable progress has been made in ensuring access to quality services throughout the laboratory network in the Region, further efforts are needed to improve result timeliness and completeness of monthly measles surveillance reports.

Important challenges remain in maintaining quality and procuring the resource needed by the measles and rubella laboratory network. These challenges include identifying funding resources for laboratory supplies for measles and rubella testing and encouraging countries to integrate these costs into their national surveillance budgets whenever possible.

Recommendations:

TAG endorses all the recommendations of the pre-TAG meeting of the Measles/Rubella Laboratory Network that took place in Guatemala on the 23 July and highlights the following:

- Laboratory testing is an integral component of measles, rubella, and CRS surveillance and countries are strongly encouraged to incorporate laboratory costs into their surveillance budgets.
- Laboratories should establish a close working relationship with epidemiologic staff to make sure that adequate specimens are collected for serology and virus isolation, and data are recorded and reported in a timely and accurate manner. Laboratory personnel should participate in national committees to discuss final classification of measles/rubella cases.
- A virus genotype should be determined for all chains of transmission of measles and rubella and rigorous efforts should be undertaken to collect specimen accordingly.
- PAHO should continue to advocate with national governments and partner agencies for continued support to the measles/rubella laboratory network as a first line of defense against importations of measles from other regions and to support the elimination of rubella from the Americas.

Polio Laboratory Network

The detection of wild poliovirus importation in several previously polio-free countries underscores risks posed to countries from failure to keep high polio immunization coverage.

Therefore, the polio laboratory network must continue to provide fast and quality results that are critical for monitoring and verifying virus circulation in the Region and the progress towards the achievement of global polio eradication. Poliovirus laboratory containment in the American Region is progressing towards completion of Phase I and work is ongoing to complete surveys and inventories.

Recommendations:

- PAHO should continue to support members countries in mobilizing resources from partner agencies necessary for continued support and maintenance of the polio laboratory network activities.
- All institutions that currently house polio laboratories must be committed to ensure technical quality and performance of all laboratory personnel to minimize the risk of infectious material spreading to workers and the environment.
- Network laboratories should submit cell sensitivity test results to the regional laboratory coordinator within 48 hours after test completion. Should there be evidence of reduced sensitivity for poliovirus detection, the lab coordinator should assist in implementing a follow-up plan.
- Poliovirus isolates should be sent to one of the three regional laboratories accredited as intratypic differentiation (ITD) laboratories (Fiocruz in Brazil, Malbrán in Argentina, and CDC in the US) within seven days of detection. The ITD test results should be reported by the ITD laboratory within 14 days after receiving polio isolates.
- To facilitate early implementation of public health interventions, laboratories must report within 24 hours all discordant ITDs and wild poliovirus results to national authorities and the PAHO regional laboratory coordinator.
- The laboratory network must continue to participate in activities to ensure completion of Phase 1 containment throughout the Region and advocate for polio containment in appropriate scientific venues and with national governments. All wild poliovirus potential materials should be destroyed.

NEW AND UNDERUTILIZED VACCINES

Several new vaccines have been developed in the last decade and several others are in the process of development. This extraordinary progress in biotechnology will provide the medical armamentarium with several new vaccines and the countries will be faced with a major challenge of incorporating them into their national immunization programs whenever warranted.

Countries are therefore encouraged to review criteria for introduction of new vaccines, and use the lessons learned from the introduction of other vaccines such as Hib and hepatitis B. Burden of disease studies and economic analysis, along with several other activities, are essential to the decision-making process. Regarding the new vaccines against rotavirus, pneumococcus, and HPV, the main activity is to prioritize the coordination of work with organizations and groups that have already developed plans for control of diarrhea, acute respiratory diseases, and cervical cancer.

Because the price of these new vaccines will be substantially higher than that of traditional childhood vaccines, the introduction of new vaccines will have to be based on evidence that they are cost-effective. To that end, PAHO is developing a methodology for the training of national immunization program managers on the evaluation of the cost-effectiveness of these new technologies. This initiative is called Pro-Vac and will be launched in September 2006, with a regional workshop to be held in Washington, D.C. (See Section on *Financial Sustainability of Immunization Program*, page 38).

The initiative of the Sabin Vaccine Institute (SVI), which presented in relation to the development of a vaccine against Hookworm, is a new paradigm for the development and introduction of new vaccines, using innovative strategies such as an early transfer of technology to an endemic country that has vaccine production capabilities, and other modalities of partnership. The vaccine against human hookworm disease presents enormous opportunities to address a public health problem caused by an important, yet neglected, disease.

Recommendation:

- Countries should conduct economic analyses to provide evidence for the assessment of the introduction of intervention measures. These analyses must follow standardized methodologies for result comparison, in accordance with the PAHO Pro-Vac initiative.

ROTAVIRUS

Rotavirus infection is the most important cause of diarrhea in children aged <5 years in the world. It is responsible for around 600,000 annual deaths and approximately 40% of hospitalizations due to diarrhea in children aged <5 years. According to available data, rotavirus causes approximately 75,000 hospitalizations and close to 15,000 annual deaths in the Region of the Americas. Disease incidence due to rotavirus is similar in developing and developed countries, but most of the deaths (80%) occur in developing countries.

Currently, 10 countries of the Region of the Americas (Bolivia, El Salvador, Guatemala, Honduras, Paraguay, Venezuela, and four English-speaking Caribbean countries) have standardized surveillance systems for rotavirus diarrhea according to the PAHO Field Guide. These countries are reporting data on a monthly basis. Data show that around 39.9% of suspect rotavirus diarrhea cases were positive in 2005, and, up to May 2006, 52.3% of cases were positive for rotavirus (Bolivia, El Salvador, Guatemala, Honduras, Paraguay, and Venezuela). Through monthly analysis, it can be observed that rotavirus presents seasonal patterns, with the winter period showing the greater percentage of positive cases. In regards to genotypes identified in the Region, the literature and surveillance of rotavirus diarrhea have shown the emergence of serotype G9. The frequency of G3 and G9 serotypes are very similar and it could be that G9 is replacing G3. Genotype P[8] is predominant in the Region. In 2005, countries reported 83.2% of suspect case with epidemiological forms and stool samples collected. For countries reporting data up to May 2006, that figure was 68.2%.

There are currently two rotavirus vaccines available on the market and licensed by their national regulatory authorities. One is being pre-qualified by WHO and results should be available by the end of 2006. The other manufacturer will likely forward its dossier for analysis next September. Brazil, Panama, and Venezuela have introduced the rotavirus vaccine during the first 2006 semester in the routine immunization schedule for children aged 2-4 months. Mexico has introduced the vaccine in selected areas of the country and will extend vaccination to the entire country by mid-2007.

At the Sixth International Symposium on Rotavirus, held in Mexico City in July 2004 by PAHO, the Sabin Vaccine Institute, the CDC, and the US National Institutes of Health, representatives from Ministries of Health agreed to look for mechanisms within national budgetary schemes to negotiate at the higher levels in order to guarantee the sustainability of existing immunization programs and the introduction of new vaccines, and requested PAHO to negotiate with suppliers to achieve affordable prices.

Recommendations:

- All countries of the Region should implement highly sensitive and standardized surveillance of rotavirus diarrhea in sentinel hospitals by the end of 2006 with the objective to characterize the epidemiological profile and burden of the disease in the Region, and obtain data allowing evidence-based decision-taking regarding vaccine introduction.
- All countries should send rotavirus diarrhea surveillance data to the PAHO regional surveillance system on a monthly basis so they can be consolidated at regional level and fed back to the member countries.

- A great proportion of hospitalized diarrheal cases do not meet the standard proposed case definition. PAHO should assist countries to better understand the standard case definition and promote wide distribution of the guidelines and training of health professionals in its use.
- Countries must assess their cold chain capacity at all levels, immunization schedules, and availability of human resources and consider training of health providers on the use of this vaccine as a prior step to its introduction.

PNEUMOCOCCUS

It is estimated that pneumococcus disease causes around 1.6 millions deaths per year, of which 800,000 occur in children aged <5 years. Rates of pneumococcus invasive disease are higher in children aged <2 years. Yet the disease also occurs in other age groups, mainly older adults.

In the article on *Pneumococcal disease and vaccination in the Americas: an agenda for accelerated vaccine introduction*⁷ published in the Pan American Journal of Public Health, it is reported that data obtained through the PAHO/SIREVA surveillance network indicate that the main serotype distribution has not changed significantly when compared to the 1993-1999 and 2000-2003 periods. Serotype 14 is most often isolated in the majority of countries. According to local information regarding serotypes, the 7-valent vaccine would cover 65% of serotypes, the 9-valent 77%, and the 11-valent 83%. Antimicrobial sensitivity has also been monitored. Penicillin resistance has increased from 14.7 % in 1993 to 30.6% in 1999 and reached 39.8% in 2000-2003.

The Region still does not have a standardized database for surveillance of pneumococcus pneumonias and meningitis. A database would improve the quality of information regarding distribution of circulating serotypes in the population. PAHO, with the collaboration of the Pneumo-ADIP, is expanding the scope of the original SIREVA project to develop a comprehensive surveillance system for pneumococcal disease and to conduct population-based studies in countries of the Region.

Recommendations:

- Based on the guidelines that will be prepared, countries should implement epidemiological surveillance of pneumonias and meningitis in children aged <5 years to assess the burden of disease and its profile in the population.
- PAHO should support the expansion of the laboratory network capacity developed with the original SIREVA project to strengthen its capacity for the serotyping of pneumococcus isolates.
- Support for pneumococcus surveillance is a top priority and the support now provided by PAHO should be sustained beyond the current two-year grant period for which resources have been made available.

⁷ García S. et al. Revista Panamericana de Salud Pública/Pan American Journal of Public Health, Volume 19, Number 5, May 2006, pp. 340-348(9)

HUMAN PAPILLOMAVIRUS

Cervical cancer persists as a significant public health problem in Latin America and the Caribbean, despite the long standing availability and application of secondary prevention (Papanicolaou smear cytology) in member countries. Every year, 86,532 new cases of cervical cancer and 38,435 deaths occur among women in the Region of the Americas, with Latin America and the Caribbean accounting for 71,862 cases and 32,639 deaths annually. In addition to these cases of invasive cervical cancer, women with low- as well as high-grade precancerous cervical lesions (dysplasias and carcinoma in-situ) also contribute to the disease burden and the high costs associated with screening, diagnosis, and treatment of this disease. Certain types of high-risk human papillomaviruses, which infect the genital tract, have been definitively identified as the etiologic agents in cervical carcinogenesis.

Two prophylactic recombinant vaccines against human papillomavirus (HPV), one bivalent and the other tetravalent, consisting of types 16 and 18, and 16, 18, 6, and 11 virus-like particles, respectively, have been developed and have undergone extensive international Phase 2 and 3 clinical trials. Both vaccines have shown excellent results with respect to their immunogenicity, safety and efficacy in preventing incident and persistent HPV infections as well as cervical cancer precursor lesions (cervical intraepithelial neoplasia). The tetravalent vaccine has also been shown to be efficacious against genital warts (condyloma acuminata) and vulvar and vaginal intraepithelial neoplasias.

Since June 2006, the tetravalent HPV vaccine was licensed in Australia, Canada, Mexico, New Zealand, Togo, and the United States for use in females, aged 9-26 years. Additionally, some of these countries have also approved this vaccine for use in males. It should be noted that the greatest protective benefit would be derived when the vaccine is administered before initiation of sexual activity. It must also be pointed that vaccination of a girl or woman who, prior to vaccination, is already infected with any of the HPV types contained in the vaccine does not confer protection against that type. Additionally, this vaccine does not treat existing disease caused by HPV types contained in the vaccine neither does it confer protection against other oncogenic HPV types not contained in the vaccine. However, there is promising new data suggesting that the vaccine may confer cross-protection against types 31 and 45. Therefore, secondary prevention remains critically important and must still be retained as part of the cervical cancer prevention tool-kit, which would also include education, risk reduction (sexual behavior modification and condom use), and vaccination.

The availability of an effective HPV vaccine represents a significant advance in the prevention of cervical cancer. However, it must be stressed that vaccination will become only one of the interventions targeting disease control. Well-organized screening programs are essential, not only for the control of cancer, but for the evaluation and surveillance of vaccinated women.

Recommendations:

- TAG acknowledges PAHO's work in taking a regional approach for the introduction of HPV vaccine and strongly recommends that it continue this process. TAG encourages countries to take all necessary steps to ensure early introduction, particularly in countries that have poor screening programs.
- PAHO should convene an *ad-hoc* meeting of experts to discuss the most appropriate strategies and effective tools for HPV surveillance in Latin America and the Caribbean.

- PAHO should support the conduct of HPV surveillance pilot projects in some selected member countries in order to demonstrate how the surveillance system would be operationalized, its costs, and the required information system.
- PAHO should continue to work with its partners and manufacturers to ensure that HPV vaccines are affordable and available equitably in Latin America and the Caribbean.
- TAG endorses the recommendations of the Second Meeting on Partnering for HPV Vaccine Introduction (Annex 1).

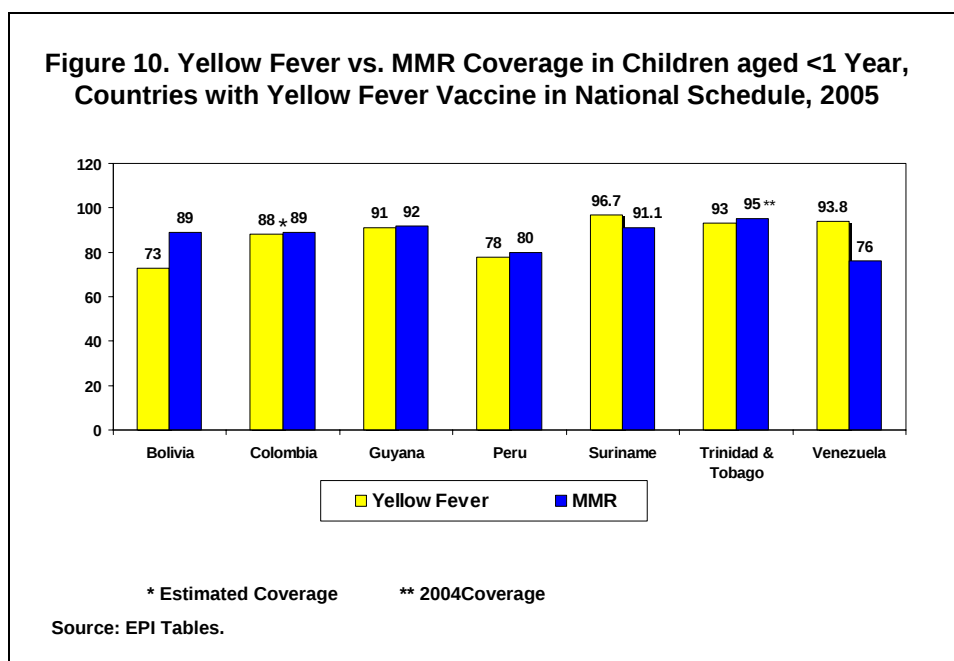
YELLOW FEVER

Yellow fever is an enzootic disease in South America. Countries with enzootic areas are Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Suriname, Trinidad and Tobago, and Venezuela.

Yellow fever presents a cyclical pattern. From 1995 until epidemiological week 9 of 2006, 3,701 cases and 1,938 deaths were reported. Three major peaks were observed, the largest one in Peru with 499 cases in 1995. In 1998, outbreaks were reported in Peru (165 cases), Bolivia (57), and Brazil (34). In 2003, case incidence increased due to outbreaks in Colombia (112 cases), Brazil (64), Venezuela (34), and Peru (26). Between 2004 and 2006, limited outbreaks and isolated cases were reported. However, reporting has been late in some instances.

The majority of countries with enzootic areas have made significant progress in yellow fever control through implementation of national plans of action including vaccination of the population residing in those areas and strengthening of epidemiological surveillance. Outbreak control measures have been adopted, including vaccination of travelers to enzootic areas. TAG recognizes and encourages continued progress in this area of work.

Seven of the 10 countries with enzootic areas that routinely report to PAHO have introduced yellow fever vaccine in their national immunization schedule for all children aged 1 year, at the same time as MMR (Figure 10).



Recommendations:

- Countries with enzootic areas should consider yellow fever a public health priority, gathering all the political, technical, and financial support to continue with implementation of national plans for yellow fever prevention and control.

- It is essential to complete vaccination of all the population residing in enzootic areas and in communities where immigration to enzootic areas originates. The strengthening of the information system and analysis is crucial to evaluate and monitor the plans in order to focus vaccination in municipalities or areas with low vaccination coverage.
- The three remaining countries that did not do so, should include yellow fever vaccine in their national schedule so the vaccine is administered at the same time as MMR to children reaching one year of age.
- Countries should continue to improve the quality and sensitivity of the epidemiological surveillance for yellow fever. In non-enzootic areas, outbreak control measures should be strengthened and include increasing the sensitivity of the surveillance system, improving the capacity for adequate outbreak response, maintaining a vaccine supply at national level, and conducting vector control to avoid re-urbanization of the disease.

INFLUENZA

Seasonal Influenza

Influenza is a viral disease that strikes millions of people worldwide and causes fatal complications in approximately one million people every year. Many of these cases and deaths can be avoided through the use of safe, highly effective vaccines. Countries in the Region are advancing in the implementation of the recommendations to increase influenza vaccination coverage in elderly people, chronically ill individuals, and health care workers, and considering additional target groups as warranted.

With the objective of determining the current status of influenza vaccination in the Region, a survey of national immunization program managers was conducted. Thirty-nine countries or territories responded to the survey. Forty-nine percent (19) informed that they have public policies for influenza vaccination, and 85% (33) reported having routine epidemiological surveillance systems for influenza. The countries or territories surveyed do not have consistent information on viral circulation patterns. Among those that already have an established national influenza vaccination policy (19), 68% (13) provided coverage data on high-risk populations, 84% (16) vaccinate health care workers, and 16% (3) immunize persons in contact with birds. Nineteen countries or territories in the Region purchased vaccine through the Revolving Fund in 2006.

Progress has been made in introducing influenza vaccination in the Region. The immunization of children aged 6-23 months has been introduced in 8 countries. Three additional countries are vaccinating children aged <5 years with high risk conditions. However, there is a limited global production capacity and countries may face recurrent vaccine shortages, mainly in regards to the Northern Hemisphere formulation.

Recommendations:

- All countries must strengthen the surveillance system to determine the burden of influenza, the cost-effectiveness of introducing influenza vaccine, and its impact, and to decide on the best vaccination strategy to use and when, particularly in tropical areas. PAHO should provide and disseminate guidelines on the use of the vaccine to countries.
- TAG recommends that all countries establish a seasonal influenza vaccination policy that aims to vaccinate with seasonal influenza vaccine children aged 6-23 months, health care workers, chronically ill individuals, and elderly adults.
- Countries using the vaccine should generate vaccination coverage data and document experiences and lessons learned from targeting high-risk groups. This will be useful for countries newly introducing the vaccine and in the event of a pandemic.
- PAHO should continue to promote mechanisms for the transfer of technology to increase Regional capacities in vaccine production and keep track of global supply.

Pandemic Influenza

TAG is pleased that PAHO is providing technical cooperation to countries for the development and implementation of national Influenza Pandemic Preparedness Plans (IPPPs) in response to Resolutions from PAHO's Directing Bodies and the Summit of Presidents of countries of the Region held in Mar del Plata in November 2005.

The high circulation in avian species of the H5N1 avian influenza virus, its establishment in enzootic form in domestic birds in Asia, Eurasia, Eastern Europe, and Africa, and its capacity to infect people on a limited basis, yet with the potential to transform into a pandemic strain, demonstrate its global magnitude. Therefore, countries must be prepared to face a pandemic due to the H5N1 strain and other strains should that occur. Epidemiological and viral influenza surveillance should be strengthened and expanded to respond to the new realities imposed by the circulation of a new avian influenza virus with pandemic potential.

Preparation for a pandemic is a continuing process aimed at strengthening basic capacities in public health, mainly at local levels where the greater impact in all sectors of the society is expected, particularly in the health sector. In addition, the strengthening of basic public health capacities, mentioned in the new International Health Regulations, will not only enhance the capacity to respond to an influenza pandemic, but also any public health emergency.

Vaccination is one of the pandemic control measures. Unfortunately, it is very unlikely for a vaccine to be available at the beginning of a pandemic since it is impossible to predict what pandemic strain will strike. Also, four to six months are required to start the influenza vaccine production process once the vaccine strain is available, and the global production capacity is very limited. Existing scientific knowledge shows that, when using conventional production in fertilized eggs with the H5N1, highly pathogenic, avian influenza strains currently circulating, three to six times more antigens are required to obtain an immunity response similar to the seasonal influenza vaccine. In addition, two doses are required to confer the necessary protection. These are all factors contributing to the limited vaccine supply, at least during the first wave of the pandemic. The development of new technologies that will increase supply are underway, but will take some years to become available.

Technical cooperation includes strengthening national capacities in the areas of detection, prevention, care, communication, and adequate response to health emergencies, including health services preparedness. As of today, 28 countries have provided at least a draft of their preparedness plans. Workshops are being developed to promote self-assessment of IPPPs in the different sub-regions. A workshop has been conducted for Central America and the Dominican Republic and another one for the English-speaking Caribbean. Workshops for the Southern Cone and the Andean Area will be held in August and September, respectively. All countries of the Region have been trained in the implementation of sentinel surveillance, laboratory diagnosis, and influenza virus characterization. Eleven countries have received training in PCR diagnostic and molecular characterization of influenza virus. PAHO is also providing support to purchase antivirals, other drugs, and personal protection equipment.

Recommendations:

- All countries should continue strengthening, updating, and implementing their influenza pandemic preparedness plans. It is essential these plans be implemented at local level. TAG

encourages countries to operationalize country plans by implementing drills with local involvement.

- PAHO should continue to hold the workshops for the preparation of national plans and stimulate the exchange of information on national preparedness through simulation exercises.

NEONATAL TETANUS

In 1989 the World Health Assembly (WHA) called for the global elimination of maternal and neonatal tetanus, which was later defined as less than one case of neonatal tetanus (NNT) per 1,000 live births in every district of every country. Ten years later, global efforts were successful in eliminating NNT in 104 out of 161 developing countries. In 2000, however, NNT was still a significant public health problem in 57 countries, a fact that resulted in a renewed push by an international coalition to eliminate the disease by 2005. The number of NNT deaths has decreased from 800,000 worldwide in the 1980s to less than 180,000 in 2002, with most of these in just 52 countries. In addition, maternal deaths due to tetanus are estimated to be 30,000 annually.

TAG recognizes the tremendous achievements of American countries in NNT elimination and wants to highlight that those few countries that still experience the occurrence of NNT cases should make special efforts to conclude this task.

After the high-risk approach was deployed in Latin America and the Caribbean in 1986, the number of reported NNT cases in the Region fell more than 50% in just the first four years. From 1986 to 2005, that number fell by more than 94%. The disease is now considered to be eliminated in the entire American Region, with the exception of some countries where the problem still persists (Table 1). The total number of districts reporting an annual rate >1 NNT case per 1,000 live births was 210 in 1995 and 16 in 2005.

Table 1. Selected Latin American Countries With NNT Cases: Districts With Cases and Districts With >1 NNT Case per 1,000 Live Births, 1995 and 2005

Countries	1995				2005			
	Total Districts	Total Cases	Districts		Total Districts	Total Cases	Districts	
			Reporting Cases	Rate >1/1000 LB			Reporting Cases	Rate >1/1000 LB
Bolivia	93	20	11	4	324	5	4	2
Brazil	4954	127	113	82	5564	10	10	7
Colombia	1020	35	27	15	1113	9	8	3
Dom. Republic	153	0	0	0	153	...	...	...
Ecuador	141	51	36	9	167	6	6	2
El Salvador	262	3	3	1	262	1	1	0
Guatemala	331	9	8	5	331	0	0	0
Honduras	293	3	3	3	298	0	0	0
Mexico	2406	67	63	18	2444	1	1	0
Nicaragua	152	4	3	1	162	1	1	0
Panama	68	1	1	1	76	1	1	0
Paraguay	211	16	16	8	232	2	2	2
Peru	1811	99	75	59	1811	2	2	0
Venezuela	287	18	12	4	287	1	1	0
TOTAL	12182	453	371	210	13224	39	37	16

... not available

A single case of NNT in the Americas should now be considered a failure of the health services, and should be subject to a thorough evaluation to determine how the case could have been averted in order to prevent new cases.

Recommendations:

- Countries should sustain the gains obtained so far. Countries that still have districts with cases must conduct vaccination in high-risk areas. Every country must maintain a high quality NNT surveillance and PAHO should encourage and support these efforts.
- All NNT cases should be fully investigated by an independent peer review board. Conclusions about the failure to prevent that case must be used as a guide to target populations to be vaccinated.
- PAHO should work with UNICEF and other partners and encourage and support Haiti to conduct a nation-wide campaign to eliminate NNT and take advantage of this activity to maintain measles-free status and eliminate rubella and CRS.

STRENGTHENING PROGRAM MANAGEMENT

Countries of the Americas have used several mechanisms for managing and supervising their immunization programs. These include periodic program evaluation, plans of action, microplans at the local level, interagency coordination committees (ICCs), national immunization advisory committees, periodic supervision, feedback to the local level that includes coverage rates and surveillance data, periodic evaluation of immunization data quality, budget line for vaccine purchase and immunization program implementation, and vaccine legislation. PAHO regularly monitors several of the components listed using the annual EPI tables for immunization data collection (now also known as *PAHO-WHO/UNICEF Joint Reporting Form* or JRF).

An analysis of selected program management components using data available at the Regional level for 2004 and 2005 found that most countries are conducting internal evaluations of their programs. Although some countries have had an international EPI evaluation, the TAG notes that the number of these important multidisciplinary program reviews has diminished. Additionally, all countries of Latin America and the Caribbean reported having annual plans of action and most also have 5-year plans; most of these plans are shared with PAHO. In 2005, 13 Latin American and 4 Caribbean countries reported having ICCs. With regards to national immunization advisory committees, 3 countries in Latin America have yet to create such committees. Most countries submitted their EPI tables in May, one month after the requested deadline. Countries that submitted the tables late were more likely to send incomplete information, usually including only coverage and/or morbidity data. Feedback to the local level, usually including at least coverage and surveillance data, seems to be adequate for countries reporting this information.

In 2002, TAG recommended that all countries use standardized supervision protocols covering program components, and that sufficient financial resources be allocated for the implementation of regular supervision. In 2004 and 2005, only about half of Latin American and Caribbean countries reported on the proportion of municipalities supervised at least once each year. Of those countries reporting, supervision took place in all municipalities in roughly 60% and 85% of Latin American and Caribbean countries, respectively.

Recommendations:

- The components included in the program management section of PAHO's EPI tables (*JRF for the Americas*) are time-tested tools and need to be fully implemented and documented by countries.
- International program evaluations should be performed in each country at least every three years.
- TAG reiterates the previous recommendation that supervision should be strengthened at all level of the health system.

ASSESSMENT OF REPORTED COVERAGE DATA QUALITY

Immunization coverage levels serve as a key measure of immunization program performance. The use of number of doses administered has been, and remains, the method of choice to assess and monitor vaccination coverage levels in the Region. However, an assessment of data consistency and denominator accuracy in national immunization coverage data reported annually to PAHO has identified certain unusual patterns in the reported data, suggesting that problems in data consistency and denominator accuracy may exist in several countries.

Efforts to improve the accuracy, consistency, completeness, and timeliness of coverage data should be a top priority of every country. The evaluation of the immunization monitoring system, in terms of these elements, can be performed using different methodologies. For example, the rapid coverage monitoring recommended by PAHO provides a quick validity check on reported coverage levels and helps direct vaccination activities.

The systematic and regular analysis of coverage data provides an opportunity to critically review the reported data to identify, explain, resolve, or correct features of the reporting system that may lead to inaccurate coverage data. Likewise, the assessment of the data on coverage available at the local level should be an integral component of supervisory visits.

Recommendations:

- PAHO should develop guidelines regarding the elements that countries should consider when monitoring data quality.
- The systematic and periodic assessment of coverage data accuracy, consistency, completeness, and timeliness should become a regular activity within national immunization programs. This assessment should be conducted within the context of regular on-going evaluation and supervisory activities.
- A work plan to follow-up on monitoring system weaknesses found should be developed and implemented, and periodic re-assessments implemented.
- PAHO should define the criteria for what is referred as “data quality” and review existing methodologies to evaluate quality of coverage data in order to prioritize their use in support of countries.

VACCINATION WEEK IN THE AMERICAS

The yearly initiative for Vaccination Week in the Americas (VWA) was endorsed by Resolution CD44.R1 of PAHO's 2003 Directing Council. VWA is based on the principles of equity, access, and Pan Americanism. This initiative provides an opportunity to strengthen the routine immunization program, reach vulnerable populations with low vaccination coverage, and promote regional and border cooperation.

Table 2. Vaccination Week in the Americas: Results to Date

	2003	2004	2005	2006 ^a
Vaccination Results (number of persons)	16,285,888	43,749,720	37,932,765	44,745,806
Number of participating countries and territories	19	35	36 ^b	40 ^c
Number of countries with integrated activities ^d	...	4	5 ^e	7

... not available

(a) As of 14 August 2006; (b) 12 countries conducted awareness campaigns; (c) 16 countries conducted awareness campaigns; (d) Vitamin A, iron supplement, antiparasitic, oral rehydration; (e) In 2005, 7,615,778 persons received vitamin A supplements and 17,695,149 children received antiparasitic drugs.

In its four years of existence, participation in the VWA has increased from 19 countries during its first year (2003) to 40 countries and territories in 2006. These countries have incorporated VWA activities into their annual operational plans.

It is also essential to stress the impact of VWA on vaccination activities from the routine program and how it has helped catch up with schedules of vulnerable populations such as children and women of childbearing age (WCBAs). In 2005, five countries reported vaccinating over 48,000,000 children aged 1-4 years who had received 0 doses of DPT/Pentavalent by age one. Colombia, Guatemala, Honduras, Mexico, and Panama reported the vaccination of over 539,000 WCBAs who had never received a Td dose. In addition to vaccination activities, VWA is an opportunity for countries to offer other health services. In 2005, Bolivia, Guatemala, Honduras, Mexico, and Nicaragua distributed 7,730,000 doses of vitamin A to children aged <5 years and WCBAs. Mexico and Nicaragua also offered antiparasitic drugs to over 17 million children.

Interagency cooperation continues to be essential for the success of VWA, including technical and financial support. The CDC, GAVI, the Canadian International Development Agency (CIDA), UNICEF, the Spanish international cooperation agency, the US Agency for International Development (USAID), the Sabin Vaccine Institute, March of Dimes, the Latin American Municipality Network, health-promoting schools, local partners such as Rotary Clubs, and other non-governmental agencies have provided support through their presence and financing of events and logistics requirements in each country. In the last four years, PAHO has mobilized more than US \$3 millions that were distributed to countries of the Region, with emphasis on priority countries.

In addition, PAHO each year helps countries with the design of a mass media campaign that includes public service announcements on radio and TV with celebrities from the world of entertainment or sports. Stickers and posters are also designed to advertise vaccination activities during the VWA, adapted to local requirements. PAHO's Public Information Office has

documented the vaccination activities in vulnerable populations, at border events, and during regional launchings.

Interagency cooperation has been a crucial component of VWA. Since 2004, 34 border launchings have taken place. National and binational launchings have been an opportunity to advocate for political commitment. Over the last two years, these events were attended by five presidents, four first ladies, ministers of health, local health authorities, and representatives from international organizations and other partners.

Emulating the experience in the Americas, the WHO Region for Europe launched its first vaccination week in October 2005, and the second one is planned for October 2006. In 2007, the vaccination week in the WHO Region of Europe will take place in April, to coincide with the 2007 VWA.

Recommendation:

- VWA should be bolstered as a Regional strategy that allows the strengthening of the regional program and reducing of immunization inequities. Efforts should continue to identify and vaccinate vulnerable populations and measure the impact of interventions in those groups.

VACCINE SAFETY

As vaccine-preventable diseases become less prevalent thanks to the implementation of effective immunization programs, greater attention must be paid to events supposedly attributable to vaccination or immunization (ESAVIs). ESAVIs must be fully investigated in order to discard them or establish a cause-and-effect relationship with the vaccine. Vaccination safety is a priority component of immunization programs. Its purpose is to guarantee the use of quality vaccines, safe injection practices, ESAVI monitoring, and strengthening of partnerships with the media. These activities are crucial to maintain the credibility of immunization programs within the community.

In recent years, PAHO has been promoting the strengthening of ESAVI surveillance systems through training, support to country investigations, and information exchange. Recently, a surveillance network of adverse events due to new vaccines has been formed: Argentina, Brazil, Mexico, Panama, and Venezuela are currently participating in this network.

In relation to specific topics, mention is made of thimerosal association with adverse events following immunization, mainly autism. In its *Immunization Newsletter*⁸, PAHO's Immunization Unit has published a summary of the literature on the topic. It was concluded that there is no evidence supporting the association and, in accordance with the recommendations from WHO's Global Committee on Vaccination Safety, PAHO recommends the continued use of thimerosal-containing vaccine in routine immunization schedules.

The definition of a safe injection is based on three essential aspects: security for the individual receiving the injection, security for the health worker, and security for the community and environment. This includes the use of disposable syringes, preferably AD syringes, the disposal of waste in safety boxes, and the adequate management of these materials for final disposal through incineration.

National regulatory agencies (NRAs) are responsible for ensuring the use of safe, and effective vaccines to support immunization programs. A new challenge for NRAs is the introduction on the market of new vaccines (rotavirus and human papillomavirus) not registered in the country of origin, nor previously used in other countries.

Recommendations:

- Countries should strengthen their ESAVI reporting and investigation systems. This will allow early detection and adequate investigation. Establishing causality and responding to the population quickly with transparency will help maintain the credibility of immunization programs.
- Cooperation at country level between the national immunization program and NRAs is essential to monitor adverse events due to new vaccines in order to better appreciate the safety of new vaccines.
- Countries that are part of the network for notification of adverse events due to new vaccines should exchange information on a regular basis so they are ready to act in case of unusual

⁸ Immunization Newsletter. Update on Thimerosal and Autism. Vol.XXVII (5), October 2005.

events or greater than expected rates. Those countries that are not yet participating in the network should do so as soon as possible.

- As one component of vaccination safety, ministries of health should ensure safe injection practices are followed.
- PAHO should support the NRAs and coordinate their efforts to conduct a full evaluation of these new products, and provide technical training to generate experience, mainly in the weakest areas within the Region's NRAs, such as evaluation of clinical studies and post-marketing surveillance.

FINANCIAL SUSTAINABILITY OF NATIONAL IMMUNIZATION PROGRAMS

New generation vaccines against killer infections will ultimately help countries meet the targets of WHO's Global Immunization Vision and Strategy (GIVS) and the Millennium Development Goals (MDGs). Countries will be challenged to sustain the gains, while completing the unfinished agenda of reaching all children, eliminating rubella, and introducing new vaccines when appropriate. To achieve the targets, countries will require substantial additional financing for national immunization programs. PAHO proposes a Regional strategy directed to:

- Reduce inequity by reaching the unreached in districts with poor coverage;
- Strive to reach mortality reduction targets toward the achievement of the MDGs and targets outlined in GIVS for diseases caused by rotavirus and pneumococcus, while strengthening information and surveillance systems;
- Support strengthened national capacity to make evidence-based policy decisions regarding vaccine introduction through strategic partnerships with key global and regional institutions;
- Transition from childhood to family immunization;
- Expand fiscal space for resource allocation to national immunization programs; and
- Attain unprecedented levels of participation in the PAHO Revolving Fund for Vaccine Procurement through clear demonstration of the benefits to countries.

National leadership in immunization and public health is at a cross-roads. Best practice in making and implementing informed decisions for public health requires policy makers to consider the usual epidemiologic, demographic, and management data. Evidence to assess the balance between economic costs of vaccination and economic savings and health benefits from disease prevention is also key to responsible decision-making.

For new vaccine introduction to contribute to overall prevention effectiveness, economic evidence must be considered together with the usual epidemiologic, demographic, and management data. PAHO's Pro-Vac Initiative will provide the tools and linkages with national centers of economic studies to strengthen immunization program capacity for evidence generation and priority setting for these new technologies. It is anticipated that this will generate greater demand for, and promote the informed use of, relevant economic studies to support policy-making at country and regional levels. This initiative consists of multiple steps of training, data collection, and development of economic analysis at country level in the context of new vaccine introduction. A workshop will take place in Washington, D.C., in September 2006 to present the theoretical framework for economic analysis, including affordability, cost-of-illness, cost-of-programs, and cost-effectiveness studies, as well as to present and discuss the main tools for economic analysis for new vaccine introduction.

The PAHO Revolving Fund has brought significant benefits to participating countries. Examples include cost savings, due to lower, uniform vaccine prices resulting from high-volume bulk purchasing agreements; increased consistency and adequacy of vaccine supply through much more accurate forecasting; and greater cooperation between immunization programs of member countries when emergencies occur. Thirty-seven countries are currently making regular use of the Revolving Fund for the procurement of up to 45 different vaccine products. In addition, the Revolving Fund is streamlining its integrated services to countries through further reducing costs of vaccine procurement, holding, distribution, and use along the supply chain. At the close of 2005, the Revolving Fund was capitalized at just over US \$34 million and total expenditures exceeded \$154 million that year. Thus, a considerable gap exists between working capital

available at any one time and the level of purchases. Introduction of new vaccines will stress the capacity of the Fund to purchase supplies needed by member countries

Now more than ever, with the opportunity of the new generation vaccines already here, Pan American cooperation through the Revolving Fund will enable this Region to continue its spectacular immunization achievements. The challenge for countries will be to increase the flow of sustainable financing to accelerate the introduction of new generation vaccines for this transition. This will require evidence to ensure that national budgetary processes recognize the true economic value of immunization; close attention to supply chain efficiency and vaccine legislation to reduce transaction costs; the development of new sources of revenue for immunization; and unprecedented levels of Revolving Fund participation to ensure safety and affordable prices. The Revolving Fund, as a highly efficient procurement agency, is positioned to continue its strategic role in strengthening the sustainability of national immunization programs throughout the Region. However, it is estimated that there will be a gap of approximately US \$14 million between now and the year 2010 in the capitalization of the Revolving Fund for PAHO to continue to support procurement of vaccines. Therefore, new mechanisms to increase its capitalization will be necessary.

On Tuesday afternoon, a meeting of PAHO's Regional Interagency Coordinating Committee for Vaccine-preventable Diseases was convened with the primary purpose of addressing the greatest obstacle to the successful elimination of rubella and CRS in the Americas: insufficient financial resources. The TAG appreciates the efforts of the ICC and endorses its recommendations (Annex 2).

Recommendations:

- Countries should use available tools and information for economic analysis to assist decision-making on sustaining national immunization programs and new vaccine introduction. Countries are encouraged to participate the planned Pro-Vac workshop in September 2006, organized by PAHO.
- Countries should assess existing health legislation and regulations to ensure that national laws:
 - promote family immunization through specific provisions including no-cost, obligatory vaccination;
 - recognize the importance of immunization within the health budget and make specific provision for purchase of vaccines;
 - contribute to low transaction costs for vaccine procurement; and
 - create a supportive environment for national vaccine production where relevant.
- Countries should assess fiscal space for new vaccine introductions and investigate new sources of sustainable funding for immunization, including new indirect taxes on consumable goods with negative health impacts.
- TAG strongly encourages countries to strengthen their participation in the Revolving Fund, benefiting from savings obtained through bulk purchasing, contributing where relevant to vaccine and syringe supply, and sharing immunization assets in times of crisis, in a spirit of Pan Americanism.

- PAHO should explore the possibilities of increasing the capitalization of the Revolving Fund through negotiations with partners, including GAVI, as well as the donation of funds from member countries.
- PAHO should continue to support regional and country efforts to reduce total vaccine supply chain costs and improve the quality and timeliness of Revolving Fund operations.
- TAG strongly supports and is pleased to learn of the recommendation of the PAHO's Executive Committee to endorse the above-summarized Regional Strategy for Sustaining National Immunization Programs in the Americas. TAG recommends that the document that will be presented to the September 2006 Directing Council meeting be expanded to include a discussion of the situation of the capitalization of the Revolving Fund for Vaccine Procurement.

ANNEXES

ANNEX 1.



Immunization Unit
Family and Community Health Area



PARTNERING FOR HPV VACCINE INTRODUCTION

Summarized Highlights of a Meeting of HPV Vaccine Partners Guatemala City, Guatemala, July 2007

On 24 July 2006, the Pan American Health Organization (PAHO) convened a meeting in Guatemala City, Guatemala, on Partnering for Human Papillomavirus Vaccine Introduction. The main objectives of this second meeting of PAHO's HPV Vaccine Partners was to provide a series of technical updates on the epidemiology of cervical cancer and HPV in Latin America and the Caribbean, the results of clinical trials related to the two prophylactic vaccines under development, the lessons learned from vaccine trials in Latin America, and the implications of herd immunity for HPV vaccine introduction. Updates were also provided on WHO's policy and program guidance for HPV vaccine introduction, issues related to HPV surveillance, and one country's perspective on HPV vaccine introduction. This meeting was attended by over 100 participants that included the invited speakers, representatives of PAHO Member States and eight agencies, and two country partners.

The key issues and messages emerging from this meeting include technical, policy, and programmatic aspects.

Technical Highlights

Cervical cancer remains a major public health problem in Latin America and the Caribbean, as the countries of this Region experience some of the highest incidence and mortality rates in the world.

The two prophylactic vaccines being developed are proving to be safe, well tolerated, and highly efficacious against persistent HPV infection and cervical cancer precursors, including high grade squamous intraepithelial lesions associated with the genotypes contained in the vaccine. One prophylactic HPV vaccine was recently approved for use in Australia, Canada, the United States, Mexico, Togo, and New Zealand.

There are a number of issues for which additional research is required and some of these include the duration of long-term immunity and the need for booster doses, vaccine efficacy in males, vaccine efficacy in populations with high HIV prevalence or immune compromising conditions, and co-administration with other vaccines. The issue of HPV vaccine types 16 and 18 conferring

some degree of cross-protection against other phylogenetically-related types also needs to be further clarified.

Policy and Programmatic Highlights

The greatest concern expressed during the meeting is the affordability of and access to these vaccines. It was recognized that if the vaccines could not be purchased by the public sector, then those populations most at risk would not have access to them. At the global level, WHO, UNICEF, and other international technical cooperation agencies must advocate with a united voice to agencies such as GAVI and the International Financing Facility for Immunization to assure equitable availability and affordable vaccine prices.

From a programmatic perspective, effective advocacy, service delivery, and sustained financing for HPV vaccine introduction also require collaborative partnerships between key stakeholders, namely, immunization, cancer control and sexual and reproductive health, at the global, regional, sub-regional, national, and local levels.

Increasing the awareness of all sectors of the population regarding HPV as a major cause of cervical cancer and ways to prevent the disease is a key requirement for building and sustaining political will. Information dissemination to a variety of stakeholders, including professional medical associations, health care providers, women's and community groups, and policy-makers is therefore an important programmatic activity.

The issue of including boys as part of the target population for HPV vaccination was also raised by several participants. Expanding herd immunity and social acceptabilities were considered to be advantages in alignment with PAHO's strategic objective to transition from child to family immunization.

Key recommendations emerging from the meeting's discussions are as follows:

- A meeting of the PAHO HPV Vaccine Partners should be convened on an annual basis in order to further consolidate and advance the partnership in support of timely and effective HPV vaccine introduction;
- PAHO should actively collaborate with its HPV vaccine partners to articulate optimal strategies for the conduct of surveillance, economic analyses, and demand forecasting in Member States. The collaboration should be supported by the development and application of appropriate tools. To this end, PAHO's ProVac Initiative should play an effective role.
- PAHO and its HPV Vaccine Partners should work collaboratively to assist Member States in exploring innovative mechanisms for increasing fiscal space in their budgets so that the introduction and sustained maintenance of the HPV vaccine is guaranteed and the platform for effective cervical cancer prevention and control is realized.
- The proceedings of this second HPV Vaccine Partners Meeting should be formally documented and used for advocacy and resource mobilization.

ANNEX 2.



Immunization Unit
Family and Community Health Area



INTER-AGENCY COORDINATING COMMITTEE GUATEMALA CITY, JULY 2006

RECOMMENDATIONS

Background

The 2006 Inter-agency Coordinating Committee (ICC) meeting took place in Guatemala City, in conjunction with the XVII Meeting of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases. Since TAG's last meeting in 2004, rubella campaigns have been successfully conducted in Bolivia, Colombia, Ecuador, El Salvador, Nicaragua, and Paraguay. The Region appears on track to achieve rubella and congenital rubella syndrome elimination (CRS) by 2010. However, the lack of resources in the remaining seven countries that need to conduct rubella vaccination campaigns is the single most important obstacle to reaching the elimination goal.

Other challenges to sustaining national immunization programs were discussed. PAHO has initiated a process of comprehensive assessment of the vaccine supply chain and Revolving Fund operations, with the objective to identify cost-savings and efficiency gains. In parallel to these activities, PAHO has also initiated with countries a review of vaccination-related legislation to identify best practices and seek legislative and regulatory mechanisms for reducing country vaccine procurement transaction costs. In addition, the Revolving Fund has sought to respond to country demand for seasonal influenza vaccine and to position itself to support the introduction of new generation vaccines, including rotavirus, pneumococcus, and human papilloma virus (HPV). These processes have highlighted critical limitations associated with current levels of Revolving Fund capitalization and identified new capital targets to ensure the uninterrupted supply of life-saving vaccines to countries of the Region.

Recommendations for the ICC:

- Mobilizing the necessary resources to support country efforts for rubella and CRS elimination, including sufficient resources for disease surveillance and mass vaccination campaigns.
- Supporting the Revolving Fund by helping to mobilize the US \$14 million needed to ensure that sufficient working capital will be available to meet future demand for vaccines in the Region.