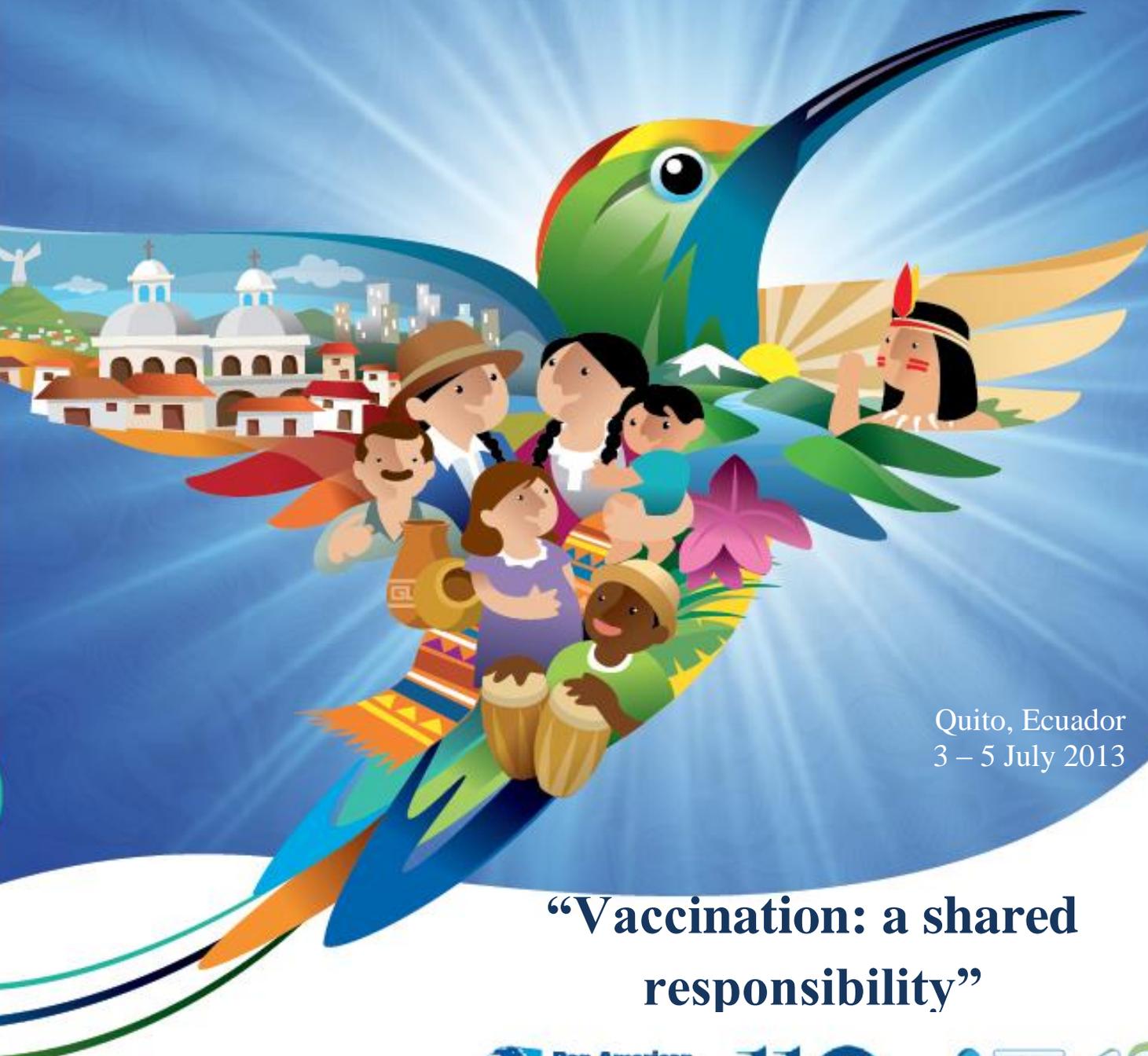


# Technical Advisory Group on Vaccine-preventable Diseases



Quito, Ecuador  
3 – 5 July 2013

**“Vaccination: a shared  
responsibility”**



**TECHNICAL ADVISORY GROUP ON VACCINE-PREVENTABLE DISEASES  
XXI MEETING: “VACCINATION: A SHARED RESPONSIBILITY”  
QUITO ECUADOR, 3-5 JULY 2013**

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## ACRONYMS

AFP	Acute Flaccid Paralysis
BCG	Bacillus Calmette–Guérin – vaccine against severe forms of tuberculosis
CDC	Centers for Disease Control and Prevention of the United States
CRS	Congenital Rubella Syndrome
cVDPV	(circulating) Vaccine-derived Poliovirus
DPT	Diphtheria-Pertussis-Tetanus vaccine
DPT3	Third dose of the Diphtheria-Pertussis-Tetanus vaccine
EPI	Expanded Program on Immunization
ESAVI	Event Supposedly Attributable to Vaccination or Immunization
EW	Epidemiological Week
GIVS	Global Immunization Vision and Strategy
GVAP	Global Vaccine Action Plan
JRF	Joint Reporting Form (PAHO-WHO/UNICEF)
HPV	Human Papilloma Virus
IBD	Invasive Bacterial Disease
IPD	Invasive Pneumococcal Disease
IEC	International Expert Committee (for the documentation and verification of measles, rubella, and CRS elimination in the Americas)
IPV	Inactivated Polio Vaccine
LAC	Latin America and the Caribbean
LAIV	Live Attenuated Influenza Vaccine
MR	Measles-Rubella Vaccine
MMR	Measles-Mumps-Rubella Vaccine
MMR1	First dose of the Measles-Mumps-Rubella Vaccine
MMR2	Second dose of the Measles-Mumps-Rubella Vaccine
NIP	National Immunization Program
NITAG	National Immunization Technical Advisory Group
NNT	Neonatal Tetanus
OPV	Oral Polio Vaccine
bOPV	Bivalent Oral Polio Vaccine
mOPV	Monovalent Oral Polio Vaccine
tOPV	Trivalent Oral Polio Vaccine
PAHO	Pan American Health Organization
PCV	Pneumococcal Conjugate Vaccine
PoA	Plan of Action
PPV23	Pneumococcal Polysaccharide Vaccine 23 -valent
REVELAC-i	Influenza Vaccine Effectiveness Evaluation Network for Latin America and the Caribbean
RF	PAHO's Revolving Fund for the Purchase of Vaccines and Immunization Supplies
RIVS	Regional Immunization Vision and Strategy



SAGE	Strategic Advisory Group of Experts on Immunization for the WHO
SIREVA	Regional Vaccine System – laboratory network for invasive bacterial pathogens
TAG	PAHO’s Technical Advisory Group on Vaccine-preventable Diseases
TIV	Tetravalent Influenza Vaccine
UNICEF	United Nations Children’s Fund
VWA	Vaccination Weeks in the Americas
WHA	World Health Assembly
WHO	World Health Organization
WIW	World Immunization Week



## INTRODUCTION

The XXI Meeting the Technical Advisory Group (TAG) on Vaccine-preventable Diseases of the Pan American Health Organization (PAHO) was held in Quito, Ecuador on 3-5 July 2013. The slogan for the meeting was “Vaccination: a shared responsibility. This meeting’s objective was to issue recommendations to address the current and future challenges faced by national immunizations programs in the Americas.

Dr. Ciro de Quadros, TAG President, chaired the meeting. PAHO’s Director, Dr. Carissa F. Etienne, addressed the participants virtually and gave a brief introductory speech. Following the Director’s video, the PAHO/WHO country representative in Ecuador gave a brief welcome. Dr. Miguel Malo, Vice Minister of Health, greeted participants and expressed how honored Ecuador felt to be hosting this important meeting.

The TAG acknowledged the contributions of PAHO’s Secretariat to the success of the meeting and thanked the Ecuadorian authorities for so graciously hosting the meeting.

## PERTUSSIS (WHOOPING COUGH)

Pertussis is a significant cause of childhood mortality globally, and as such, it has been a topic for discussion in the last three TAG meetings. Recommendations made during these meetings include the need for strengthening of epidemiological surveillance; the administration of a 4<sup>th</sup> dose as part of the routine vaccination schedule; starting diphtheria-tetanus-pertussis (DTP) vaccination at 6 weeks of age and vaccinating pregnant women only during outbreaks; and carefully replacing the whole-cell pertussis vaccine with the acellular vaccine, while the duration of immunity conferred by acellular vaccines is still being evaluated.

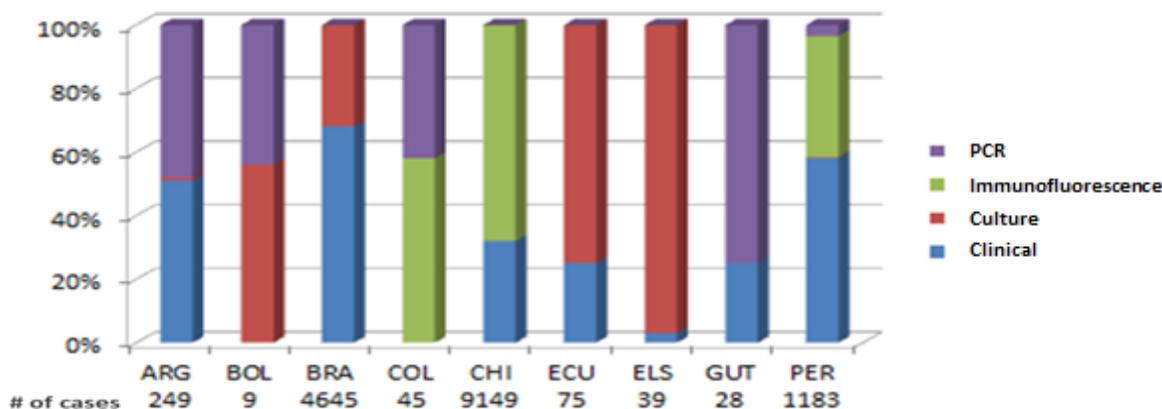
Following previous recommendations, the regional pertussis epidemiological situation, the recommendations of the World Health Organization's (WHO) Strategic Advisory Group of Experts on Immunization (SAGE), evidence on the duration of the protection conferred by acellular vaccines, and the conclusions of the PAHO/WHO Pertussis Working Group were presented during this meeting.

**Figure1.** Countries that have had pertussis outbreaks over the last 3 years (2010 – 2013)



After holding two meetings and gathering information from Latin American and Caribbean countries (LAC), the Pertussis Working Group prepared a guidance document on Investigating and Reporting of Pertussis Outbreaks. In this document, the Group reported that: a) with the exception of Cuba, Costa Rica, Dominican Republic, Haiti, Honduras, Mexico, Nicaragua, and Venezuela, every Latin America country, as well as Canada and the United States, has reported pertussis outbreaks during the last 3 years; b) in 2012, the pertussis incidence rate (per 100,000 inhabitants) ranged from 0 (zero) in Cuba to 33.8 in Chile; c) the case-fatality rate varied widely, for example, in 2012 in the Dominican Republic it was 18%, in Paraguay 9%, in Honduras 6%, in Mexico 5%, in Brazil 1.5% and in Chile 0.2%; d) in countries that reported outbreaks, 42% of the cases involved infants under 6 months of age; e) eight countries use a general definition of pertussis cases, while nine have specific definitions by age group; f) some countries continue using immunofluorescence as a laboratory diagnostic method, despite the fact that its use is no longer recommended; and g) some countries reported numerous outbreaks, some with only two or three cases each.

Figure2. % of pertussis cases by confirmatory method by country. Selected Latin American countries, 2010-2012



The TAG appreciates and commends the efforts of countries in the Region, for preparing detailed information on the epidemiology of the outbreaks (case definitions used, sex and ages of cases, confirmation method, laboratory tests, signs and symptoms and relevant outcomes, such as hospitalization and death) for the first time. It should be noted that the high proportion of children under 6 months of age in the outbreaks could indicate an over diagnosis in that age group or an under identification of cases in other age groups. The great disparity in the incidence rates reported in the continent are difficult to explain between countries that have comparable vaccination schedules and coverage. The high proportion of deaths to the number of cases could only be due to an inadequate case management or the small number of cases captured by surveillance systems.

Information currently available on the duration of immunity conferred by acellular vaccines was presented during the meeting. This information continues to show that duration of immunity is



shorter than that of the whole-cell vaccine. Meanwhile, SAGE has asked its own Working Group to continue gathering epidemiological evidence to facilitate decision-making.

The recommendation of the October 2012 meeting of the United States Advisory Committee on Immunization Practices (ACIP) was also presented. In that meeting, ACIP recommended administering one dose of the Tdap vaccine during each pregnancy, regardless of the number of previous doses a patient has received. This dose should be administered between weeks 27 and 36 of pregnancy for the purpose of optimizing the transfer of antibodies to the newborn. If it is not administered during pregnancy, it should be administered in the immediate postpartum period. In order to estimate the potential impact of this strategy, a model showing that this strategy could prevent 9 deaths (ranging from 4-17) was used. The number of deaths recorded annually among children >12 months of age from 2000 to 2011 was 18 (ranging from 8-35).

The TAG reviewed the outputs of the Working Group, which include the guidelines and forms for outbreak monitoring and reporting, and expects them to serve as an input and stimulus for countries to gather epidemiological evidence for better decision-making.

## RECOMMENDATIONS

- Countries using current vaccination schedules with whole-cell pertussis vaccines should continue to do so. There is marginal and insufficient benefit to consider changing from whole-cell pertussis-containing vaccines to acellular pertussis-containing vaccines.
- Countries should continue striving to provide timely vaccination and achieve coverage levels  $\geq 95\%$  with pertussis-containing vaccines in all municipalities.
- All countries should strengthen pertussis surveillance to better monitor the epidemiology of the disease. Countries should continue assessing the quality of their surveillance systems in order to evaluate the reliability of their data on incidence, case-fatality, age distribution, proportion of cases confirmed by different methods, and vaccine effectiveness.
- Countries should use the guidelines proposed for investigating all outbreaks, to allow national programs and TAG to continue evaluating the epidemiology of pertussis on an ongoing basis.
- TAG reiterates its previous recommendations related to outbreaks. These recommendations include lowering the age for initiating vaccination to 6 weeks and vaccinating pregnant women **only** in areas affected by the outbreak. Currently, there is no evidence for TAG to recommend routine vaccination of pregnant women.



## EVIDENCE BASED DECISION-MAKING FOR NEW VACCINE INTRODUCTION

New vaccines are considerably more expensive than traditional vaccines, and their introduction into national immunization programs in the Region imposes greater resource requirements. Given that national budgets for immunization are slow to expand relative to the needs of the programs, the scarce resources available must be used as efficiently as possible, and mechanisms should be sought to protect them. Arguments for increasing national immunization budgets must be strongly grounded in evidence given the many other existing public health priorities. The Global Vaccine Action Plan approved during the 2012 World Health Assembly, calls for the incorporation of evidence assessment into immunization policy-making with the aim of maximizing health impact and efficient resource use.

Recognizing this need, PAHO established the ProVac Initiative in 2004 with the goal of strengthening national capacities for evidence-based decision-making around new vaccine introduction, with a particular focus on the use of economic evaluations in the decision-making process. In 2006, the ProVac Initiative was officially endorsed by PAHO's Governing Bodies through resolution CD47.R10. Then, in 2009, the ProVac Initiative was awarded a five-year grant by the Bill & Melinda Gates Foundation to support country decision-making around new vaccine introduction. In 2010, the ProVac Network of Centers of Excellence was formed, including academic institutions in Latin America with expertise on economic evaluations to develop tools and guides for countries conducting economic studies with local and regional data. Thus far, over 25 economic evaluations and costing studies have been conducted by multidisciplinary national teams in 15 countries. The cornerstone of all technical assistance provided by the ProVac Initiative has been the bolstering of national capacities, South-South cooperation, and country ownership of the process of evidence generation.

Argentina is one of the countries in the Region that has achieved remarkable advances in the institutionalization of an evidence based decision-making process for new vaccine introduction with support from the ProVac Initiative. In addition to performing 3 nationally-based cost-effectiveness analyses on new vaccines over the last 5 years, they have also improved the operating procedures of the National Immunization Technical Advisory Group (NITAG) and added a full-time Ministry of Health professional solely devoted to generation and collection of evidence to aid immunization policy-making.

These efforts to strengthen national capacities in the Americas have gained global recognition and have led to repeated requests for support by other WHO Regions. Accordingly, in 2012 PAHO was awarded an additional grant to provide time-limited support for the use of economic evaluations in immunization decision-making in select countries of Africa, Europe, and the Eastern Mediterranean. This work is being carried out in collaboration with international partners: Agence de Médecine Préventive (AMP), PATH, CDC, Sabin Vaccine Institute and WHO headquarters, regional and country offices.

Despite these important steps that countries have taken thus far, much remains to be done to incorporate evidence into the immunization decision-making process. Countries must strive to create a broad, nationally based evidence framework for their decision-making, one that will consider not only technical criteria but also programmatic, financial, and social criteria. Countries



have successfully used cost-effectiveness analysis as an initial framework for generating information about new vaccine introduction related to the anticipated incremental program costs and projected cost savings from health service visits and hospitalizations averted. However, these data do not provide much guidance on logistical, financial, or social concerns, such as equity. While countries undoubtedly recognize the importance of incorporating these other criteria into national immunization decision-making, there is a need for additional tools and guidance on how to evaluate all these criteria—technical, programmatic, financial, and social.

The Region of the Americas has always been a pioneer and a global leader in immunization. These achievements are now potentially at risk due to the increased complexity of the decision-making and planning that must be undertaken by the national immunization programs (NIPs). New vaccine adoption without an adequate evidence base and careful planning could lead to an overall decrease in performance of the NIPs. The Programs could start facing problems of underfunding and inefficiencies, resulting in decreased public health benefits. This would also affect other health programs that benefit from the structure and reach of the national immunization programs to provide additional health services and interventions.

#### *Proposal to tackle these challenges*

To ensure that NIPs are equipped with the necessary capacities to meet decision-making challenges, a three-pronged approach is proposed.

- I. *Expand the evidence base beyond cost-effectiveness:* The technical aspects of immunization policy-making should always be balanced with the programmatic and social aspects and should be considered in the context of the health system overall. In particular, the Region of the Americas is affected by the crippling effects of inequities within countries, in health and other areas of life, and immunization policy should aim to redress some of these inequities. Other dimensions that countries should include in their policy evaluations include assessing how the new vaccine could prevent high out-of-pocket health care expenditures and assessing subnational variations in the likely impact of the new vaccine.
- II. *Institutionalize an evidence-based decision-making process for new vaccine introduction:* Institutionalization of NITAGs or similar technical advisory bodies, through ministerial decree or national law, is advisable to ensure continuity of policy recommendations and to establish explicit relationships between the advisory bodies and government agencies. These legal frameworks should also ensure financial support to carry out relevant research and operational studies to inform national immunization policies. Technical working groups should be formally established to expand the national evidence base, further cementing the infrastructure necessary to have a comprehensive, national, evidence-based decision-making process.
- III. *Integrate policy-making and planning for NIPs:* Policy decisions followed by successful planning for adoption of new vaccines into national routine immunization schedules requires collaboration between several actors and harmonization of processes that have generally been treated separately. Integration of costing, budgeting, and planning processes and their accompanying tools will ensure that the incorporation of new vaccines in the routine program generates positive and sustainable results. The integration of these



processes can be supported by existing ProVac tools and methodologies and by technical cooperation from PAHO's regional immunization program.

This approach is proposed as the basis for the work plan of the ProVac Initiative in its second phase, which is planned for the period 2014 to 2019.

## RECOMMENDATIONS

- TAG recognizes the National Immunization Programs in the Region for their efforts in incorporating economic evidence into new vaccine policymaking processes.
- TAG commends the efforts and achievements of the ProVac Initiative in providing technical support to Member States for more informed decisions around new vaccine introduction.
- TAG recommends that PAHO Director and Member States provide their support for a future phase of the ProVac Initiative which will address issues related to equity and societal financial risks and the institutionalization of an evidence based decision-making process.
- TAG encourages the ProVac Initiative to continue sharing lessons learned around the evidence-based decision-making for new vaccine introduction with other WHO Regions.



## YELLOW FEVER

Yellow fever continues to be a significant public health problem for the 13 countries of the Americas with endemic areas. Over the last thirty years, yellow fever virus activity has been restricted to the enzootic area shared by Bolivia, Brazil, Colombia, Ecuador, French Guyana, Guyana, Panama, Peru, Suriname, Trinidad and Tobago, and Venezuela. Since late 2007, the Region has experienced intense circulation of the yellow fever virus with extensive epizootics and outbreaks of human cases. The endemic area was extended to include Paraguay and northern Argentina, because of human cases and epizootics detected in 2008.

The main mode of transmission of yellow fever in the Americas is the sylvatic cycle. However, in 2008, cases of yellow fever were reported in the metropolitan area of Asuncion, Paraguay. Prior to this, the last confirmed urban outbreak of yellow fever in the Americas had occurred in 1942 in Brazil. This event, in addition to the proliferation of *Aedes aegypti* in the Region, shows the high risk of re-urbanization that still exists in the Americas.

From 1985 through 2012, countries have reported 4066 cases and 2351 deaths from yellow fever in the Region, with a 58% fatality rate. During this period, 95% of the cases were reported by 4 countries: Peru with 54%, Bolivia with 18%, Brazil with 16% and Colombia with 7% of the cases, respectively. French Guyana, Guyana, Panama, Suriname and Trinidad and Tobago have not reported cases in more than two decades.

The yellow fever vaccination strategies used in the Region of the Americas include: 1) introduction of the yellow fever vaccine in national immunization programs for children 1 year of age<sup>1</sup> in every country with endemic areas; 2) vaccination campaigns during inter-epidemic periods; 3) vaccination campaigns in response to outbreaks or epizootics, and 4) administration of the vaccine to those traveling to areas where there is a risk of transmission of the yellow fever virus, except for those for whom vaccination is contraindicated.

As of 2012, every country in the Region with enzootic areas has added the yellow fever vaccine to their national immunization schedules. In Argentina, Brazil and Panama, the vaccine is only administered in areas with potential risk. Vaccination coverage of children 1 year of age in countries where yellow fever is endemic, which is approximately 70% for the period from 2007 to 2012, has been significantly affected by insufficient availability of the vaccine. This shortage of yellow fever vaccines places the achievements attained by the Region at risk, with regard to the strategy of vaccinating children one year of age, as well as the vaccination of susceptible individuals living in high-risk areas.

In 2013, the SAGE revised its 2003 position paper on the use of the yellow fever vaccine. This revision placed special emphasis on whether the need exists for a booster every 10 years and on vaccine safety in special populations such as the population  $\geq 60$  years of age, individuals infected with the human immunodeficiency virus (HIV), other immunosuppressed individuals, pregnant women and infants. SAGE's main recommendations are the following:

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<sup>1</sup> Brazil recommends the administration of this vaccine at 9 months of age.



1. A single dose of the yellow fever vaccine is sufficient to confer sustained immunity and lifelong protection against the disease. Therefore, no booster is required.
  - a. However, surveillance should be intensified and clinical studies should be conducted to determine whether specific risk groups (for example, patients infected with HIV) require a second dose.
  - b. The International Health Regulations need to be revised in order to make the necessary adjustments to the validity period required for international yellow fever vaccination certificates.
2. Regarding use of the vaccine for individuals  $\geq 60$  years of age, SAGE indicated that while the risk of vaccine-associated viscerotropic disease is greater than in younger groups that receive the vaccine, the overall risk is still low.
  - a. Vaccination of individuals  $\geq 60$  years of age who have not been previously vaccinated and require it, should be recommended based on a risk-benefit evaluation in which the risk of contracting the disease is weighed against the risk of a potentially serious adverse event following vaccination.
3. The yellow fever vaccine is contraindicated in seriously immunosuppressed individuals (including those with conditions such as thymus disorders, symptomatic HIV, malignant neoplasms under treatment, treatments with immunosuppressants or immunomodulators, recent transplants, current or recent radiation therapy). The vaccine can be offered to individuals with asymptomatic HIV infection with CD4 counts  $+ \geq 200$  cells/mm<sup>3</sup> that require vaccination.
  - a. It is recommended that the vaccine be administered to all clinically healthy children through routine vaccination programs, and that HIV tests not be a prerequisite for vaccination in this context.
  - b. It is recommended that in situations in which the risk of yellow fever is high and large-scale vaccination campaigns are conducted, it is not necessary to determine HIV infection as a requirement for immunization.
4. Vaccination of pregnant and breastfeeding women
  - a. Pregnant women that reside in enzootic areas: vaccination is only recommended in the case of outbreaks, as well as in any situation in which there is an apparent risk of yellow fever transmission (preventative campaigns), because the risk of transmitting the virus from the vaccine to the fetus is less than the benefits of vaccinating pregnant women.
  - b. Breastfeeding women that reside in enzootic areas: vaccination is recommended because the risk of transmitting the virus from the vaccine to the infant is less than the benefits of vaccinating breastfeeding women.



- c. Pregnant or breastfeeding women that travel to endemic areas: vaccination is recommended when the trip cannot be postponed or avoided. They should receive counseling on the benefits and potential risks of vaccination so that they can make an informed decision. The benefits of breastfeeding are far superior to those of other nutritional alternatives.
5. Simultaneous administration of yellow fever and measles vaccines. A number of studies have indicated that yellow fever and measles vaccines can be administered simultaneously without affecting the safety or immunogenicity of the yellow fever vaccine; however,
  - a. A study showed that simultaneous administration of the yellow fever and measles, mumps and rubella (MMR) vaccines in children suggest that immunogenicity may be compromised for both the yellow fever vaccine and the rubella and mumps components of the MMR vaccine. However, to date, the evidence is insufficient to change current recommendations. Therefore, the simultaneous administration recommendation stands.
  - b. SAGE recommended conducting additional studies on simultaneous administration of the yellow fever vaccine and others.
6. The strategy to control yellow fever should include surveillance and yellow fever vaccination through a combination of routine immunization strategies and large-scale disease-prevention campaigns. Campaigns in response to outbreaks should be conducted if vaccine coverage is inadequate in the population.

## RECOMMENDATIONS

- TAG endorses the recommendations issued by SAGE:
  - One yellow fever vaccine dose is sufficient to provide sustained immunity and life-long protection against the disease, therefore no booster is required.
  - In regards to special populations, immunocompromising conditions including symptomatic HIV or CD4+ counts  $< 200$  cells/mm<sup>3</sup> are contraindications to vaccination while age  $\geq 60$  years, pregnancy, and breastfeeding are precautions to vaccination. A risk-benefit analysis is recommended for individuals with a precaution to vaccination.
  - The recommendation for the simultaneous administration of MMR and yellow fever is maintained, given that to date there is no sufficient evidence to change current recommendations.
- TAG calls for further studies to better understand the potential need for boosters in special groups, as well as the simultaneous administration of yellow fever and other live vaccines such as MMR in children. Also, additional studies are needed on the immunogenicity and safety of yellow fever vaccine in persons aged  $>60$  years, HIV-infected adults and children, and pregnant and breastfeeding women.



- TAG reemphasizes the importance of yellow fever vaccination through the routine immunization program and of maintaining high coverage levels in order to prevent cases and outbreaks of the disease.
- PAHO should work towards addressing the long-standing issue of insufficient yellow fever vaccine supply in the Region through technology transfers and other mechanisms. Similarly, TAG strongly urges PAHO, WHO, partners, and vaccine manufacturers to develop a strategy to increase the global production capacity for yellow fever vaccine.



## VACCINATION DURING EMERGENCY SITUATIONS

Natural disasters and acute humanitarian emergencies are unforeseen events that can result in large movements of people, overcrowding, poor sanitation, disruptions in the supply of clean water, limited access to food, and damage to the health infrastructure. These conditions favor the emergence of communicable diseases like diarrheas and respiratory illness, including pneumonias, primarily affecting children and seniors. In some situations of natural disasters or mass violence, there can be a significant number of injured people. In situations like disasters, the question of whether to vaccinate, what vaccines to use, when and the scope of vaccination often emerge. For many years, PAHO's Immunization Program has issued recommendations regarding vaccination in disaster situations. The main objectives of these recommendations are to prevent outbreaks of vaccine preventable diseases (VPD), particularly of those with a high morbidity/mortality; to prevent tetanus cases in injured patients; and to reestablish routine immunization as soon as possible. The latest update to these recommendations was issued in 2010, following an earthquake that affected Haiti.

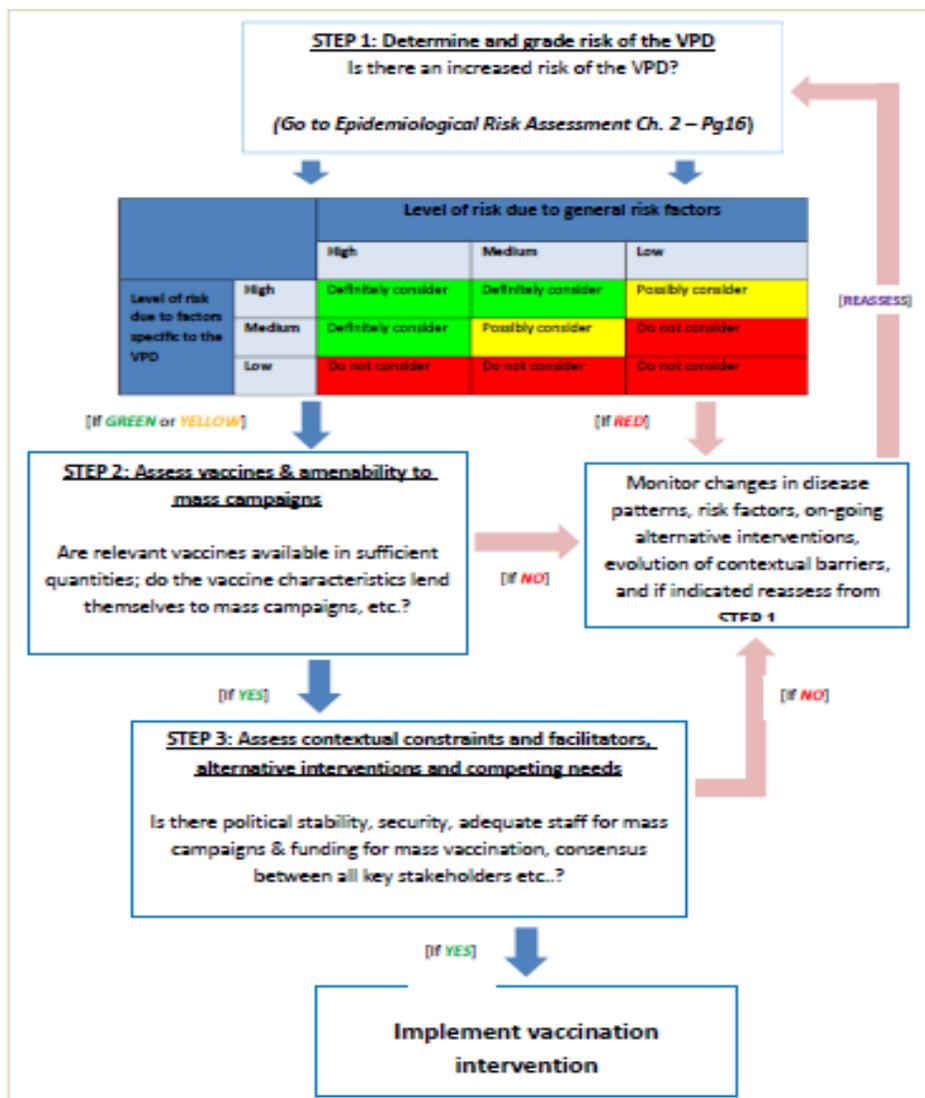
In 2011, the WHO's SAGE on Immunization of established a Working Group on Vaccination in Humanitarian Emergencies to review the available evidence on the current decision-making processes for vaccination in humanitarian emergencies. After conducting an exhaustive literature review and a review of current practical experiences with the decision-making processes for vaccination in these emergencies, the Working Group concluded that there was limited guidance for making decisions regarding vaccination in emergencies that was widely accepted or generally used. For example, the guidelines most widely used by humanitarian response agencies to respond to these emergencies are Sphere<sup>2</sup>. On vaccination, these guidelines used to only recommend measles vaccination among children between 6 months and 14 years of age, the provision of vitamin A supplements and the provision of critical vaccines and supplies, such as cold chain equipment, and experts on training and social mobilization. In an effort to fill this gap, the Working Group developed "Vaccination in Acute Humanitarian Emergencies: a Framework for Decision-Making". This framework was endorsed by the SAGE in 2012.

The framework for decision-making on vaccination in acute humanitarian emergencies was developed for national authorities and partner agencies to use, and it proposes a standardization of the decision-making process in 3 steps. These steps are shown in the following diagram:

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<sup>2</sup> The Sphere Project is a voluntary initiative that brings a wide range of humanitarian agencies together around a common aim - to improve the quality of humanitarian assistance and the accountability of humanitarian actors to their constituents, donors and affected populations. The Sphere Handbook, Humanitarian Charter and Minimum Standards in Humanitarian Response, is one of the most widely known and internationally recognized sets of common principles and universal minimum standards in life-saving areas of humanitarian response. See more at: <http://www.sphereproject.org/about/#sthash.KiyVzJ59.dpuf>





In light of this new framework for decision-making on vaccination during acute humanitarian emergencies; of polio eradication being declared an operational emergency at the 2012 World Health Assembly; of the regional progress towards measles and rubella elimination and the emergency plan to maintain elimination of these diseases endorsed by the 2012 PAHO's Directing Council; and considering recent updates to WHO positions papers on some vaccines, notably cholera, yellow fever, hepatitis A, pneumococcal and meningococcal, PAHO has reviewed its recommendations and presented them to the TAG prior to dissemination. In these recommendations, countries are urged to adopt the decision-making framework for vaccination in acute humanitarian emergencies. PAHO's recommendations also summarize considerations on vaccines that could be used, highlighting polio and measles-rubella vaccination. Furthermore, they reiterate that mass vaccination is not always recommended in the wake of a disaster and that it could even be counterproductive. They cite which vaccines to be considered for disaster and



humanitarian emergency response teams, and emphasize the importance of reestablishing the routine immunization as soon as possible. These recommendations are included in Annex A.

#### **RECOMMENDATIONS**

- The TAG adopts the SAGE Working Group's Framework for Decision-Making on Vaccination in Acute Humanitarian Emergencies and endorses the recommendations of PAHO's Immunization Program (Annex A).



## PROGRESS ON HUMAN PAPILLOMA VIRUS VACCINE INTRODUCTION & FRAMEWORK FOR IMPACT EVALUATION

Countries in Latin America and the Caribbean are increasingly introducing vaccines against human papillomavirus (HPV) in their national immunization schedules. In July 2011, four countries had included the HPV vaccine in their schedules and 2.6 million girls (34% of an adolescent female cohort typical for the Region) had access to HPV immunization. In July 2013, ten countries have included the HPV vaccine in their schedules and 4.5 million girls (58%) have access to HPV immunization.

While progress in HPV vaccine introduction over the past two years is notable, obstacles to a wider adoption by other countries of the Region persist. First, together with PCV, the HPV vaccine remains the most expensive EPI vaccine in the Revolving Fund intended for potential universal use. Vaccine cost is also perceived as unaffordable and sometimes as unfairly priced. Second, public health priorities in Latin America and the Caribbean often focus on childhood killers (pneumonia and diarrhea) and maternal mortality and, consequently, public investments are directed at their prevention. Finally, health professionals express uncertainty about safety and long-term efficacy of HPV vaccines, its delivery strategies, and the possible integration with cervical cancer screening.

The HPV vaccine is safe, but public and some health professionals continue to have concerns regarding HPV vaccine safety. In June 2013, WHO Global Advisory Committee on Vaccine Safety reviewed updated information about the safety of HPV vaccines. Based on that information and considering that more than 170 million doses have been distributed worldwide and more countries are offering the vaccine through national immunization programs, this Committee concluded that it continued to be reassured by the safety profile of the currently available HPV vaccines. The characteristics of today's HPV vaccines, the data generated in the large clinical trials and post-marketing surveillance (both with passive and active systems), and the efforts are all important considerations supporting such a conclusion.

Where the vaccine has been introduced, programmatic challenges remain in accurately measuring vaccination coverage and in integrating HPV immunization with other health programs for adolescents and cancer programs. HPV vaccination coverage data frequently show drop-out rates as high as 50%. It is currently difficult to determine whether those data reflect problems in HPV vaccine acceptance, in information systems, or both. As evidence accumulates on the effectiveness of HPV vaccines, the fulfillment of the potential of HPV immunization eventually rests in achieving and maintaining high vaccination coverage for all doses of the schedule.

The expectation that HPV immunization could lead to integration with, and consequently achieve greater access, to cancer programs, school health programs, and sexual health programs, has generally not happened. Integration is often reduced to joint communication campaigns that advocate for vaccination of adolescents and cervical cancer screening in adult women. However, Argentina started HPV DNA testing in the Province of Jujuy (with plans for a gradual nation-wide expansion) as part of a comprehensive cervical cancer prevention program and Uruguay is offering the HPV vaccine in health centers within the framework of sexual health programs. Both experiences are very promising.



Mexico and the two Canadian Provinces of British Columbia and Quebec have adopted immunization schedules that differ from the schedules licensed by regulatory agencies between 2008–2010. In these alternative immunization schedules, intervals between the administration of the first and subsequent doses are extended (second dose given at 6 months and the third dose given at 60 months after the first dose). As of July 2013, no cohort has reached an age when the administration of the third dose is expected and it is thus unknown whether vaccinated girls can be reached again five years after administration of the first dose. Colombia switched to an extended 3-dose schedule in the first semester of 2013 and the national TAG of Chile recommended the HPV vaccine introduction with similarly extended schedules. Immunological, programmatic and financial advantages are the rationale for alternative schedules. Clinical trials indicate that the immunogenicity of two HPV vaccine doses in adolescent girls is not inferior to the immunogenicity from three doses in young women through 36 months of follow-up. Post-hoc analysis of the data from a clinical trial conducted in Costa Rica suggests high efficacy for a less than 3-dose schedule. Additional evidence on alternative schedules can be expected over the next few years.

At its previous meeting, the TAG recommended that PAHO develop a framework to monitor HPV occurrence and to evaluate the impact of HPV immunization in the Region. The proposed framework outlines primary and complementary endpoints that can be monitored over three subsequent periods following a HPV vaccine introduction. On the short-term (5–10 years after vaccine introduction), prevalence of HPV genotypes in sexually-active adolescents is the primary monitoring endpoint, and, if the quadrivalent vaccine were introduced, prevalence of genital warts could be a complementary endpoint. On the medium-term (10–15 years after vaccine introduction), prevalence of precancerous lesions (with adjustment for screening coverage) and/or HPV genotype prevalence in invasive lesions are primary endpoints; cervical cancer screening coverage and positivity of screening tests could be complementary endpoints. On the long-term ( $\geq 20$  years after vaccine introduction), cervical cancer incidence or mortality and HPV genotype prevalence in invasive cancer are primary endpoints; incidence of other HPV-related cancers, cervical cancer screening coverage, and follow-up of women with positive screening tests could be complementary endpoints. Rather than being prescriptive, this framework illustrates different options that Countries can adopt depending on the specific national and local conditions. Activities developed within the regional framework may have a positive influence on national programs for cervical cancer screening.

## RECOMMENDATIONS

- Countries which have introduced HPV vaccine should strengthen their efforts to characterize vaccination coverage at subnational and national levels.
- TAG also recommends that countries, which are considering an introduction, carefully plan information systems to collect and analyze coverage data at all levels.
- TAG endorses the June 2013 statement of WHO Global Advisory Committee on Vaccine Safety related to HPV vaccine and recommends that PAHO disseminate evidence of HPV vaccine safety in the Region.
- Countries should, depending on their capacities, adopt the activities laid out in the regional framework for impact evaluation of HPV vaccine. TAG recognizes that a regional network of HPV laboratories is an integral component of such a framework.



- TAG recommends 2- and 3-dose extended HPV immunization schedules for girls aged 9–13 years as they can offer immunological, programmatic and financial advantages. TAG also recognizes the need to gather data on a longer term for 2-dose schedules.
- PAHO should continue to explore mechanisms to make the HPV vaccine more affordable without compromising the principles of the Revolving Fund.



## LABORATORY MEETING REPORT

The Regional Laboratory Network of the Americas has been providing support for vaccine preventable disease (VPD) eradication, elimination, and control initiatives as soon as they have been approved by the Pan American Sanitary Bureau since 1986, when the US Centers for Disease Control and Prevention (CDC) and PAHO conducted the first training of country personnel and established the Polio Lab Network. The first training of measles-rubella laboratories in countries took place in 1995. This strategic alliance between the CDC and PAHO continues to this day and has enabled the strengthening of Regional Laboratories' responses to VPD surveillance, providing important and relevant information for decision-making and the steering of national immunization programs.

The aim of the Laboratory Network is to have national laboratories with sufficient response capacity available to support VPD surveillance, to confirm the presence or absence of pathogens and to generate high quality, timely and reliable results.

The Laboratory Network's role is based on: a) providing timely and precise information that allows for the confirmation or discarding of suspected/probable VPD cases; b) identifying the serotypes, serogroups, genotypes and patterns of transmission; c) providing reliable information that allows tailoring of resources towards control, elimination, and eradication of diseases, as well as, documenting the impact of new vaccine introductions; d) providing the capacity and ability to respond to unusual events; and e) advocating to national authorities on the need to continue strengthening laboratories and improving the services they provide.

Among the Laboratory Network's main accomplishments are:  $\geq 98\%$  of reported AFP cases had specimens analyzed by one of the network's laboratories; the timelines of laboratory results for polio has been reduced from 42 days to 28 days and currently to 21 days for viral isolation and intratypic differentiation; the Regional measles-rubella Laboratory Network has documented the Region's endemic genotypes and has confirmed the presence of imported cases in a timely fashion; the burden of rotavirus disease has been established and the circulating genotypes have been identified in various countries in the Region; surveillance of bacterial pneumonias and meningitis, through SIREVA and SIREVA II, has documented the main circulating serotypes/serogroups; recently, there has been an expanded participation of laboratories in Global External Evaluation Programs (3-polio, 2-measles-rubella, 1-rotavirus, 1-invasive bacterial vaccine preventable disease or IBVPD) that reveals the laboratories' technical capacity; and the building of capacities and training of lab personnel on new tests has been kept current.

The main challenges identified within the Regional Laboratory Network are related to: a) reaching and maintaining quality standards and surveillance indicators; b) guaranteeing national commitment, as sometimes laboratory surveillance is not considered a national priority; c) maintaining trained personnel as limited numbers of trained laboratory personnel and the permanent migration of personnel that exists; d) having adequate equipment given limited availability of equipment and reagents to implement new tests; e) providing timely response, noting that the usefulness of laboratory results is based on their reliability and on the timeliness in which they are communicated to the surveillance system; f) resource mobilization for all events under surveillance;



g) difficulties with customs/national authorities for specimen referrals and for receiving proficiency panels; and h) maintaining the support of groups from experts and strategic partners.

The need to consider the feasibility and relevance of establishing a Network of VPD Laboratories arises in response to the advent of new vaccine introductions that require the addition of new labs and new diagnostic methods. This Network would ideally guarantee that lab services necessary for the surveillance of these events are rendered; it would optimize management and communication of and with the different stakeholders in the system.

Lab participation in the Polio Eradication and Endgame Strategic Plan (2013-2018), recently defined by the WHO, is closely related to the plan's Objective 1: Detect and interrupt all poliovirus transmission. It requires a strong commitment, participation and compliance with performance indicators for polio labs to guide this final phase and consolidate the global eradication of poliomyelitis.

Moreover, at the Regional level, labs have had a strategic role during the verification of measles, rubella, and congenital rubella syndrome elimination phase. For this reason, the well-functioning of the Regional Laboratory Network should be kept current and its sustainability guaranteed.

TAG acknowledged the efforts and commitment of the Regional Laboratory Network in support of the eradication, elimination and control of vaccine preventable disease. Furthermore, it congratulated the national laboratories in the Region for their accomplishments and invites them to continue strengthening the essential role that labs play and to continue developing response capacities

## RECOMMENDATIONS

- Laboratories within the Network should harmonize the different procedures used to identify serotypes/serogroups/genotypes of the different VPD causing pathogens, in order to facilitate the comparability of lab results between countries and optimize the availability of data in all countries of the Region of the Americas.
- TAG reiterates that surveillance and labs are essential components of an effective immunization program and that they are required for strategic and evidence based decision-making. For these reasons, TAG urges countries to improve the integration of information generated by labs with those of the surveillance system.
- TAG recognizes that there is a need to establish a Regional Network of Vaccine Preventable Disease Laboratories that would generate reliable results, under the implementation of standardized tests and quality assurance programs, to facilitate decision-making in health and support impact evaluations of new vaccine introductions.
- PAHO should analyze the possibility of procuring reagents and diagnostic kits for vaccine-preventable disease surveillance through the Revolving Fund.



- TAG endorses the recommendations issued during the meeting of the Regional Vaccine Preventable Disease Laboratory Network held in Quito, Ecuador on 2 July 2013 (Annex B).



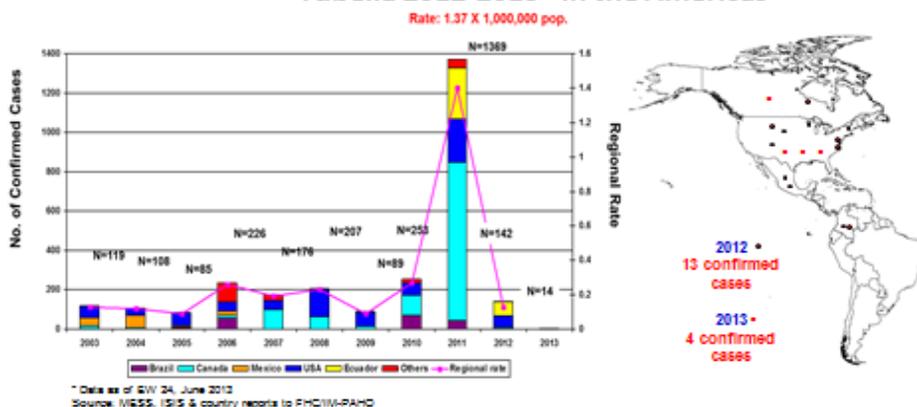
## MEASLES, RUBELLA & CONGENITAL RUBELLA SYNDROME

The countries of the Americas have demonstrated indisputable progress on the interruption of the endemic transmission of the measles and rubella viruses. Since 2002, the Region of the Americas has achieved and maintained elimination of measles and the last case of endemic transmission of rubella was reported in 2009. Continued circulation of the measles virus in other regions of the world has had an impact on the epidemiology of measles in the Americas. Following the annual occurrence of 89 to 249 imported cases and cases secondary to importation since 2003 and a large increase in cases reaching 1369 in 2011, the number of confirmed cases decreased to 142 cases in 2012 (Figure 1). All of the measles cases in 2012 were linked to importations and were reported by the following seven countries: Argentina, 1; Brazil, 2; Canada, 10; Colombia, 1; Ecuador, 72; United States of America, 55; and Venezuela, 1. Most outbreaks in the Region have been linked to the genotypes of imported viruses D8, D4 and B3; the most common is B3, mainly due to several secondary cases reported in Ecuador.

Starting in 2009, there have been imported cases of rubella. During 2012, 13 cases were reported (Figure 1), 5 were associated with importation and 8 had an unknown source of infection. Canada, Colombia and Mexico reported 2 cases each, and the United States reported the remaining 7 cases. In the cases in the United States and Mexico, the genotypes detected were 1E and 2B.

In 2012, 831 suspected cases of congenital rubella syndrome (CRS) were reported, 3 imported cases were confirmed. These cases were detected in the United States in infants whose mothers came from Africa, where the rubella virus is endemic.

**Figure 1. Distribution of confirmed cases of measles 2003-2013\* and rubella 2012-2013\* in the Americas**



Integrated epidemiological surveillance of measles/rubella met nearly all of the performance indicators for 2012, over 80%, with the exception of adequate investigation. However, the quality of active epidemiological surveillance is not homogenous at the sub-national and local levels. Nonetheless, countries have responded well to reported cases of measles and rubella, carrying out additional activities such as searching for cases, locating contacts, and evaluating risk.



There are some gaps in the surveillance of CRS; where they exist, countries use alternative and complementary lines of evidence.

This year and in the coming years, the Region of the Americas is the venue of a number of large-scale events at the national and international levels, including the 28<sup>th</sup> World Youth Day 2013 in Rio de Janeiro, Brazil, the 9<sup>th</sup> World Games 2013 in Cali, Colombia, and the 2014 FIFA World Cup and the 31<sup>st</sup> Summer Olympic Games in 2016, both in Brazil. This raises the possibility of the importation of the measles and rubella viruses from other regions of the world, which could lead to outbreaks, and at a high cost in terms of health, placing the maintenance of the elimination of these diseases at risk.

### ***Regional progress on the verification of the elimination of measles, rubella and CRS***

At the 28th PAHO/WHO Pan American Sanitary Conference, held in September 2012 in Washington, D.C., the International Expert Committee (IEC) presented progress made in the documentation and verification process to the Member States. In its regional report, it concluded that “it appears that the interruption of endemic measles and rubella virus transmission has been achieved.” However, the report establishes that “as part of the documentation and verification process, several Member States have identified challenges they need to overcome for maintaining elimination of measles, rubella and CRS. In addition, some countries have reported weakness and failures in their national surveillance systems and routine immunization programs, which must be dealt with.”

In light of the Region’s vulnerability and risk, at the Pan American Sanitary Conference, the IEC presented a plan of action for maintaining the elimination of measles, rubella and CRS in the Region of the Americas, which was approved by the Member States by means of resolution CSP28.R14. In this resolution, countries are called upon to strengthen active surveillance of measles, rubella and CRS; to ensure measures for responding in a timely manner to viruses and imported outbreaks; and to maintain 95% or more immunization coverage at the national level and in every municipality.

In order to achieve 95% or higher coverage with two doses of the MMR or measles-rubella (MR) vaccine, many countries offer a second dose of the vaccine (MMR2) in follow-up campaigns. In order to determine the timing of these campaigns, the accumulation of susceptible individuals is monitored. When the number of susceptible individuals is nearly equivalent to a cohort of newborns, which generally occurs every 4 or 5 years, a follow-up campaign is conducted.

A second opportunity to vaccinate against measles and rubella prevents the accumulation of susceptible children to dangerous levels, as some older children may not have been vaccinated or developed the disease and remain susceptible. There are a growing number of countries that have introduced MMR2 to their national routine immunization schedule, but many of them are not reaching 95% coverage. Countries have recommended different ages for administering MMR2. In 2012, 42/47 countries and territories in the Americas reported that they are administering the MMR2 in their routine program. In 32 countries (76%), it is administered to children from 3 to 6 years of age, in 5 countries (12%) from 15 to 18 months of age, in 2 countries (5%) at 2 years of age, in 2 other territories (5%) at 9-12 years of age and in 1 country (2.4%) at 6-7 years of age. During 2011, these countries and territories reported higher coverage for the first dose (MMR1)



(94%), recommended at one year of age, than for MMR2 (83%). Bolivia, Guatemala, Haiti, Honduras and Nicaragua reported that they had not introduced MMR2 in their routine schedule.

In order to maintain the elimination of measles and rubella, coverage >95% with two doses of MMR or MR is required. In light of this situation, countries should review and take advantage of programmatic considerations that make it possible to achieve high coverage and the highest immunity of the population with the MMR2. They should take advantage of every opportunity when children receive treatment, other child health interventions and simultaneous administration with other vaccines. For example, administration of the MMR2 at the age of 15-18 months of age ensures early protection of the individual and slows the accumulation of susceptible children. Therefore, it lengthens the period between one campaign and another. The MMR vaccine can be administered simultaneously with other vaccines in the routine program (for example, the DTP booster). Currently, coverage rates for DPT4 tend to be higher than those for MMR2. It should be noted that if school enrollment is high (> 95%), reviewing completion of the schedule at school entry can be an effective strategy for achieving high coverage and prevention of outbreaks in the schools. Diversity in MMR2 schedules in the Region limits monitoring of susceptible individuals and the addition of data for determining regional coverage with the same precision as the MMR1.

In May 2013, the fourth meeting of the IEC was held jointly with the 23 national commissions and a sub-regional commission from the British Caribbean in order to:

- 1) follow-up on progress made on the documentation and verification of elimination,
- 2) know the results of IEC members' country visits and the status of the national documents presented by the countries,
- 3) identify obstacles and challenges to maintaining the elimination of measles, rubella and CRS in the Region, and
- 4) discuss the implementation of the Regional Plan of Action for maintaining the elimination of measles, rubella and CRS and the work plan for 2013-2014.

The report on the meeting, which was presented to the TAG, includes general recommendations, with specific recommendations for some countries and the PAHO Secretariat. IEC members will continue making visits to countries where maintaining elimination remains a major challenge.

#### *Laboratory network*

For the purpose of analyzing the performance and challenges of the Measles and Rubella Laboratory Network, a meeting was held in May 2013 with the participation of experts from regional reference laboratories for measles and rubella for the Region of the Americas, including Fiocruz (Brazil), the National Microbiology Laboratory (Canada), the CDC and the Caribbean Public Health Agency (Trinidad and Tobago), as well as PAHO immunization professionals. Representatives of national laboratories and the WHO global laboratory coordinator participated virtually. Recommendations made during the meeting were presented to the TAG.



In view of the efforts made to verify and maintain the elimination of measles, rubella and CRS, the TAG wishes to congratulate the members of the IEC, the countries and their national commissions. Likewise, it congratulates and thanks the members for helping the Region of the Americas demonstrate that measles and rubella can be eliminated and sustained over time.

It also commends Ecuador and its healthcare workers for the efforts made to control the outbreak of measles, to demonstrate the interruption of the virus transmission and to maintain the elimination of measles in the Region of the Americas.

#### **RECOMMENDATIONS:**

- The TAG commends countries for their efforts in maintaining measles and rubella elimination and encourages countries to continue implementing its previous recommendations in order to maintain the elimination of measles, rubella and CRS.
- TAG endorses the IEC recommendations, made at the fourth joint meeting with representatives of the national commissions, and urges countries to implement them and to submit their final verification reports by 01 December 2013.
- With the goal of achieving the highest MMR2 coverage possible, administration of the MMR2 vaccine is recommended at 15-18 months, and can be given simultaneously with other vaccines, such as the first DPT booster.
- Countries should continue to verify vaccination status at school entry and immunize children who have not been vaccinated with MMR2.
- Countries should continue with high-quality follow-up vaccination campaigns in order to guarantee a high level of immunity, while the Region continues with the verification process and vaccination coverage  $\geq 95\%$  has been achieved with two doses of MMR or MR in the routine program.
- PAHO Governing Bodies and Member States should continue advocating for measles and rubella elimination in global forums such as the World Health Assembly considering that importations of the virus pose a challenge for maintaining elimination in the Americas.
- PAHO should support country efforts to systematize the lessons learned from the recent measles outbreaks and to share them with other countries of the Americas as well as with the rest of the world.



## VACCINES UNDER DEVELOPMENT: UPDATE ON DENGUE, TUBERCULOSIS AND MALARIA VACCINES

Dengue occurrence remains at historic highs. In 2012, 1,120,902 dengue cases were reported in 43 countries and territories of the Americas. Of those cases, 32,748 cases (2.9%) were severe and 784 (0.07%) case-patients died. Reported cases only represent a fraction of dengue virus infections. A comprehensive modeling effort estimated 13.3 million apparent infections (confidence interval: 9.5–18.5 millions) and 40.5 million unapparent infections (30.5–53.3 millions) for 2010. Since 2004, an increasing number of countries have adopted a PAHO-recommended prevention and control strategy that integrates case management, vector control and social communication. No antiviral drugs or vaccines are available to treat or prevent dengue.

While research on dengue vaccines has faced unique challenges, two dozen vaccine candidates are currently in preclinical development and five in clinical development. The latter are designed to protect against infections from all four dengue viruses (tetravalent vaccines); three candidates are chimeric live-attenuated vaccines and two are inactivated or subunit vaccines. In October 2012, preliminary results of the phase IIb trial of the lead vaccine candidate (CYD-TDV, a chimeric live-attenuated tetravalent vaccine) were published. This trial is being conducted in a Thai district among 4,000 children aged 4–11 years and is meant to provide the first results on efficacy. The results show safety and immunogenicity against all four dengue viruses. However, efficacy was statistically not significant (30.2%; 95% confidence interval [CI]: -13.4%–56.6%) and differed by serotype. Phase III trials for the CYD-TDV candidate are ongoing (including in Brazil, Colombia, Honduras, Mexico and Puerto Rico) and their results will eventually be critical for a CYD-TDV licensure.

In anticipation of the potential licensure of a dengue vaccine, PAHO initiated a project to strengthen national dengue surveillance systems so that they can generate the information necessary to define vaccination strategies and to evaluate their impact in November 2012. The project's specific objectives are to create a regional working group that provides input to Technical Advisory Groups on Immunization on dengue prevention and control and on vaccine-preventable diseases, to harmonize case and diagnostic definitions used in national surveillance systems, to propose a regional surveillance model, and to strengthen the regional laboratory network. HIV/AIDS, tuberculosis (TB), and malaria also cause a considerable health burden in the Americas. For our region, 170,000 new HIV infections and 96,000 AIDS-related deaths were estimated for 2010. Likewise, 260,000 incident tuberculosis cases were estimated for 2011, and 490,000 malarias cases were confirmed in 2011.

Significant research efforts have been dedicated over the past decades toward finding vaccines against these diseases, but at the present time no vaccine is available except for the 90-year-old BCG vaccine (which offers an unreliable protection against pulmonary TB). Similar challenges are faced in the development of vaccines against HIV, TB and malaria. These challenges include the need to target various components of the immune system, attempts to induce humoral and cell-mediated immune responses, and knowledge gaps in the correlation between immunogenicity and protection. Multiple HIV vaccine models are being researched concurrently. Since 1987, more than 30 vaccine HIV candidates have been tested in >80 phase I/II clinical trials; two phase III trials have been carried to completion and a third one is in progress. The RV144 HIV vaccine trial was the first and still only study to demonstrate efficacy for an HIV vaccine. This trial



included 16,395 participants from rural areas in Thailand and used a combination of two vaccines with one vaccine given in four doses and then "boosted" by two further doses containing both vaccines. Results presented in 2010 showed a 31.2% vaccine efficacy ( $p = 0.039$ ). Although this efficacy was insufficient to pursue licensure of the vaccination approach, several trials are incorporating lessons from the RV 144 trial and, if the adequate efficacy can be shown in the ongoing trials, an HIV/AIDS vaccine could become available from 2020.

A tremendous progress in TB vaccine development happened over the past decade and a rich pipeline of vaccine candidates is researched today. Twelve candidates are currently evaluated in clinical trials, of which two preventative vaccines—the MVA85A vaccine and M72/AS01 vaccine—are in phase IIb clinical trials. The MVA85A vaccine is designed to boost the immune responses that have been primed by the BCG vaccine. Results at two-year follow-up carried out in South Africa among 2,797 children aged 4–6 months were published in February 2013. Efficacy against tuberculosis was 17.3% (95% CI: -31.9%–48.2%) and against *M. tuberculosis* infection was -3.8% (95% CI: -28.1%–15.9%). Several reasons may explain the lack of protection in young children and it is still hoped that protection may result in older children, adolescents and adults. Phase IIb trial results for the vaccine M72/AS01 are not available yet. International partners devised a strategic blueprint to introduce the safest and most effective vaccines worldwide over the decade. Assuming that one of the most advanced vaccine candidates shows sufficient efficacy, the first new TB vaccine since the 1920s could become available by 2020.

While only one candidate for *Plasmodium vivax* malaria vaccine is in clinical development, several *P. falciparum* vaccines are tested in clinical trials. Among the latter candidates, the lead candidate RTS, S/AS01 is being studied in a phase III trial conducted in seven African countries. At one-year follow-up, the estimated vaccine efficacy against all clinical malaria episodes was 33.0% (95% CI: 26.4%–38.9%) in children vaccinated at ages 6–12 weeks and 55.1% (95% CI: 50.5%–59.2%) in children vaccinated at ages 5–17 months. An expert committee, which reports jointly to WHO's SAGE and Malaria Policy Advisory Committee (MPAC), reviewed these phase III trial results and considers that several questions remain unanswered, such as how efficacy changes over time after immunization, by transmission intensity, and seasonally. As long as further data and analyses become available, a joint session of SAGE and MPAC may make malaria vaccine policy recommendations in the last quarter of 2015.

## RECOMMENDATIONS

- TAG recognizes PAHO's work toward the harmonization of dengue surveillance systems across countries in the Americas and recommends that all countries contribute and participate in this effort.
- PAHO should support national regulatory authorities in defining harmonized regulatory pathways for the licensure of dengue vaccines.
- TAG considers important that, once licensed, dengue vaccine is not only made available to larger countries in the Region but also to smaller countries, if they so choose.
- TAG recognizes that several institutions in countries of the Americas, beyond Canada and the United States, have made great contributions to the development of new vaccines but



still represent largely untapped potential. International efforts should be undertaken to strengthen and coordinate research in vaccine development across the Americas.



## PNEUMOCOCCAL VACCINATION IN ADULTS

Pneumococcal pneumonia and other diseases caused by *Streptococcus pneumoniae* continue to be a substantial cause of morbidity and mortality worldwide. Pneumonia is the most common manifestation in adults, and bacterial pneumonia is the most common form of invasive bacterial disease (IBD), accounting for 90% of the total number of cases. Mortality associated with pneumococcal pneumonia has hovered around 25% globally in recent decades.

The epidemiology of pneumococcal disease in adults in developing countries is not well described, but it is acknowledged that the burden of disease globally is significantly underestimated. In addition, the burden of pneumococcal disease has increased due to the number of individuals with chronic diseases or infected with HIV, as well as the aging of the population in many countries. Drug resistance, which is the greatest obstacle to the successful treatment of infections, has also been on the rise. In industrialized countries, fatality from pneumococcal bacteremia can reach 15-20% among adults and 30-40% in older adults, even when patients receive appropriate antibiotic therapy and intensive care.

Currently, there are two vaccines available in the market for use in adults: the 23-valent pneumococcal polysaccharide vaccine (PPV23), (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F), licensed since the 1980s for the population > 2 years of age, and the 13-valent (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23 F) pneumococcal conjugate vaccine (PCV), licensed in 2013 for use in adults over 50 years of age. Both vaccines are considered safe and well tolerated.

Many studies have been conducted on the effectiveness of the PPV23 in healthy adults and adults with risk conditions since this vaccine was licensed. The results of these studies are not consistent and there is considerable controversy regarding the efficacy in the different population groups against different outcomes studied (invasive pneumococcal disease – IPD, pneumonia, mortality, etc.), in the context of childhood PCV vaccination.

The 2012 WHO position paper mentions the meta-analyses performed on the studies on efficacy and effectiveness of the PPV23, among them a meta-analysis and review of the randomized controlled clinical trials (RCTs) conducted by Cochrane Database Systemic Reviews and published by Huss A et al. in the Canadian Medical Association Journal. These meta-analyses demonstrate that the results of the RCT on the PPV23 are compatible with a protective effect against IPD and all-cause pneumonia in young adults with overall good health and, to a lesser extent, protection against IPD in the elderly population in general. These RCTs have not demonstrated that the PPV23 is effective against IPD or all-cause pneumonia in populations with greater risk, such as adults and children with underlying conditions that increase the risk of contracting pneumococcal disease or highly immunosuppressed individuals of any age.

Many studies underscore the possibility that IPD rates will remain high among people for whom the PPV23 is recommended, partially due to low coverage with this vaccine, because of its limited effectiveness in populations with risk conditions and the potentially short duration of immunity.



More recently, immunogenicity studies have been conducted for the 13-valent PCV in adults. These studies have shown good immunogenicity, especially for the serogroups included in the vaccine.

In many industrialized countries, the incidence of adult IBD has decreased sharply with the introduction of childhood pneumococcal conjugate vaccines, including age groups that are not the primary vaccination target group, due to the herd immunity effect these vaccines provide.

## RECOMMENDATIONS

- PCV should be introduced in the routine vaccination schedule for children and high coverage should be maintained. PCV not only protects vaccinated children, but also protects other age groups as a result of herd immunity.
- Countries should establish high quality epidemiological surveillance of pneumonia and invasive bacterial diseases in adults and the elderly, at sentinel sites, to better understand the epidemiological profile of the disease in these age groups and to measure the herd effect of the conjugate vaccines used.
- The available evidence does not support the use of PPV23 in adults with risk factors due to the questionable effectiveness of the vaccine in preventing pneumococcal disease in this risk group.
- Countries currently using PPV23 in adult populations should consider conducting strategic research to contribute to the understanding around the value this vaccine.
- At this time, TAG does not recommend the use of conjugate pneumococcal vaccines for all adults. Introduction of PCV in adults should be grounded in evidence and decisions should not be based on the availability of donations or other factors.



## SEASONAL INFLUENZA VACCINATION

The Region of the Americas has made considerable strides in the introduction of the seasonal influenza vaccine. Among the main criteria used by the countries are TAG and WHO recommendations, and cost/effectiveness studies in countries such as Colombia and Costa Rica, among others.

By 2012, 41 of the 46 countries and territories were using the seasonal influenza vaccine in the public sector to protect one or more risk group. This includes 39 countries and territories that vaccinate the elderly; 37 have vaccinated healthcare workers, 30 vaccinate children, and 34 that vaccinate individuals with chronic diseases. It is important to note the progress made in the vaccination of pregnant women. As of 2008, only seven countries were vaccinating pregnant women against seasonal influenza. Following the H1N1 pandemic, there has been a rapid increase in the number of countries vaccinating this group, which grew from 7 to 22 countries in the last two years.

Although significant progress has been made in the introduction of the influenza vaccine in the majority of countries, there are still challenges such as a few effectiveness studies on the vaccine in LAC. Given that effectiveness of the influenza vaccine varies depending on age, risk group and a match between vaccine strains and strains circulating annually, it is necessary to systematically know the performance of the vaccine and to have evidence for adequate decision-making in public health.

During 2012, a pilot phase was carried out in four Central American countries in order to evaluate the effectiveness of the influenza vaccine in a collaborative project between the CDC, TEPHINET and PAHO. In a technical meeting on influenza held in the city of Antigua, Guatemala on February 25-27, 2013, in which representatives of 12 LAC countries and technical cooperation research centers and agencies participated, a network (REVELAC-i) was established to evaluate the effectiveness of the influenza vaccine in Latin America and the Caribbean. For 2013, in addition to the Central American countries, the participation of countries such as Argentina, Brazil, Colombia and Paraguay, among others, is expected.

Despite generalized use of the vaccine, other significant challenges such as the following remain:

- Quality and completeness of coverage data – lack of trustworthy denominators and variability in definitions of risk groups.
- Low level of acceptance of the vaccine by healthcare personnel.
- Operational challenges to complete two-dose schedules for children <9 years of age vaccinated for the first time.
- Seasonality in tropical countries.
- Coordination between vaccination, epidemiology and laboratory programs.



- Purchase of seasonal influenza vaccines, outlook, formulation and timely delivery of the vaccine due to production processes.
- Inserts for vaccines contain precautions or contraindications for vaccination of pregnant women, which presents an obstacle to vaccination of this priority group.

### ***SAGE Recommendations***

During the SAGE meeting held in November 2012, it was recommended that countries using or considering the introduction of the seasonal influenza prioritize 5 groups, with pregnant women as the group with top priority. In addition, the vaccination of 4 other groups was recommended in no particular order: children under five (particularly ages 6-23 months), healthcare workers, the elderly and individuals with chronic diseases. SAGE also placed special emphasis on the fact that countries should individually take into account the burden of disease and cost-effectiveness, feasibility and seasonality studies, in order to make evidence-based decisions on groups to prioritize and when to vaccinate.

*Pregnant women* have a high risk of severe complications and death. This risk is exacerbated by the presence of co-morbidities. Infection in pregnant women causes complications in the fetus, including low birth weight, fetal death or child mortality. The effectiveness and safety of the TIV has been demonstrated for the mother and the child. (Children under 6 months of age have high rates of hospitalization associated with influenza.)

*Children under five*, especially children 6-23 months of age, experience a high burden of disease due to influenza. Protection of this immunologically naive group requires two doses of the vaccine, and its effectiveness particularly depends on a match between vaccine strains and circulating viruses. Children from 2–5 years of age also have a high burden of disease, although lower than the under 2 years of age group, and may respond better to influenza vaccines.

*Healthcare workers* are at greater risk of contracting influenza than the population at large. In this group, the vaccine not only protects the individual, but also vulnerable patients, and may reduce absenteeism from work. Immunization of healthcare workers should be considered as part of a broad hospital infection control program.

*Seniors (or older adults)* have a greater risk of serious disease and mortality associated with influenza, due to which they continue to have high priority for vaccination. Although evidence shows that the vaccines are less effective, they continue to be a very important measure, due to the high vulnerability of this group.

*People with chronic diseases* include groups at high risk for influenza as well as those with HIV, asthma, and cardiac and lung diseases.

The current influenza vaccines are trivalent inactivated influenza vaccines (TIV) or live attenuated influenza vaccines (LAIV). They include two A strains and a B strain. Inactivated vaccines are the only ones licensed for children from 6 to 24 months of age, people over 50 years of age, and pregnant women. There are also quadrivalent vaccines (2 A strains and 2 B strains) that have been licensed or will be soon (LAIV, IIV).



The TAG commends the countries for efforts made in the Region in relation with vaccination against seasonal influenza, especially the vaccination of high risk groups such as pregnant women, among others. In addition, it applauds the formation of the first network of developing countries for the purpose of evaluating the effectiveness of the influenza vaccine, which is a multicentric, collaborative effort with support from PAHO, CDC and TEPHINET.

## RECOMMENDATIONS

- TAG reiterates its and SAGE's previous recommendations on the vaccination of high risk groups against seasonal influenza, with special emphasis on pregnant women. Due to the vulnerability of pregnant women to complications from influenza infection, countries should strengthen vaccination of pregnant women.
- Countries should increase vaccination coverage in healthcare workers and identify the reasons for non-vaccination in this group in order to try to reduce these obstacles.
- Countries should improve the quality of coverage data on the influenza vaccine in high-risk populations, including the standardization of denominators.
- TAG encourages countries to continue evaluating the effectiveness and impact of the vaccine, which entails an effort to strengthen epidemiological surveillance, as well as immunization and laboratory programs.



## PROGRESS AND CHALLENGES ON NATIONAL VACCINATION REGISTRIES

Countries in the Americas continue making progress towards the development and implementation of immunization registries. Mexico, Panama (though not throughout its entire territory), Uruguay, and some Caribbean islands are using national immunization registries. Belize, Brazil, Chile, Colombia, Costa Rica and Guatemala are undergoing a gradual implementation process and facing diverse challenges. Argentina, the Dominican Republic, Honduras and Paraguay are in development and piloting phases; while El Salvador and Venezuela have recently begun advancing towards an immunization registry. In the case of Canada and the United States, existing immunization registries are kept by province, state or jurisdiction. This list does not include immunization registries used by sub-national levels in Latin American countries, or registries used by other entities such as non-governmental organizations, social security systems, among others.

The immunization registries have followed a variety of approaches in terms of their development and maintenance, financing, data entry model (vaccinator vs. data entry clerk) and online and offline versions. Similarly, some registries are independent, while others are part of larger health information systems. Some registries are related with other immunization information systems, such as vaccine and supply logistics management systems or tools for epidemiological surveillance of vaccine preventable diseases and events supposedly attributable to vaccines and immunization (ESAVIs). However, as is no data that would enable the comparison of the advantages and disadvantages of the different approaches used, it is currently impossible to determine which is the most effective and efficient model.

There is evidence indicating that measuring vaccination coverage better, results in improved coverage levels. National immunization registries facilitate monitoring coverage by cohort and geographical area, allowing for the individualized follow-up on increasingly complex schedules and identification of individuals with delayed or incomplete schedules, and facilitate sending automated recall/reminders. If an immunization registry is complete, its data could be used as denominators to calculate coverage. Registry data can be triangulated with census projections. Furthermore, the rosters can be contrasted periodically, using capture-recapture techniques, with birth rosters or other data sources. This is already being done by some immunization programs using a registry. Nominal immunization registries are a key tool for monitoring vaccination coverage in each community, which is a goal established in the Global Vaccine Action Plan approved by the World Health Assembly in 2012. The implementation of these registries is facilitated by the increasing availability of new information and communication technologies (ICTs), as well as the rapid increase in availability of computers and connectivity.

As more countries develop and implement this type of registries, lessons learned continue to emerge. Highlighted among these is the fact that the implementation of an immunization registry cannot be seen as a project, but rather should be considered a process that will take time and will need to be monitored and accompanied. Furthermore, the registry will require continuous human and financial resources for its maintenance and proper use. Similarly, it has become evident that in order for a system to be accepted and the data entered be of good quality an immunization registry should not only obtain vaccination coverage rates for managerial use, it should be useful to vaccinators and facilitate work at the operational and local levels. Finally, there is a need to evaluate existing national immunization registries and the experiences of their development and



implementation – in terms of effectiveness, costs, and impact on the efficiency of workflows – in order to distil and standardize best practices and lessons learned.

Other challenges for developing and using national immunization registries include: a) costs, not only those incurred during the development phase but those incurred for maintenance and for continuous updates and improvements; b) issues related to policies for data security and privacy of personal information; c) the need for registries to be flexible enough to accommodate new vaccines, new schedules and special situations; d) the need for training, which in some cases goes as far as to teaching how to use a computer; e) its acceptability at the various levels, but primarily at the operational level; and f) practical issues such as the best forms for capturing data, how to manage duplicate records and correct and timely synchronization of databases for offline registries. The Region of the Americas is at a crucial point with regard to the use of immunization registries. It will be important to disseminate and share experiences and lessons learned on this topic in order to pave the way for countries that are developing an immunization registry or considering one.

## RECOMMENDATIONS

- Recognizing the progress made on the development and implementation of computerized nominal immunization registries in the Region, TAG reemphasizes its previous recommendations on the topic.
- Countries should monitor the implementation of an immunization registries to ensure that they perform properly and, if necessary, implement timely corrective actions.
- Vaccination registries should always meet the needs of vaccinators at the local level.
- PAHO should assess country experiences on immunization registries and continue fostering the exchange of country experiences, lessons learned and good practices at the regional and global level.
- PAHO and countries should explore the use of innovative mobile technologies linked to immunization registries, where applicable.



## PROGRESS OF HAITI'S IMMUNIZATION PROGRAM

The Expanded Program on Immunization (EPI) is a priority of the Haitian Ministry of Public Health and Population (MSPP). The EPI is focused on reducing morbidity and mortality due to vaccine-preventable diseases, as well as maintaining the elimination of polio, measles, rubella and congenital rubella syndrome (CRS). Despite commendable progress made recently (such as the implementation of intensive child health activities), the EPI still faces significant challenges in some of its components.

In this regard, the MSPP, with on-going support from strategic immunization partners and based upon the multi-annual plan for 2011-2015, developed a 2013 work plan for the purpose of strengthening regular immunization services in the country. PAHO is supporting this work plan by providing technical and financial support to strengthen management and coordination of the EPI, the organization of regular vaccination services, the logistics system, the cold chain, communication, social mobilization, the introduction of new vaccines and epidemiological surveillance.

### *Progress to date*

#### *Vaccination coverage*

Historically, vaccination coverage for the different antigens has been low, without surpassing the 80% mark. However, starting in 2011, vaccination coverage began to improve progressively, particularly with BCG (82%) and the third dose of DTP3 (85%), which indicates improvement in access to vaccination services at the local level. Sustaining this progress is the greatest challenge facing the EPI in Haiti. In 2012, coverage levels fell to 69 and 80% respectively (see Table 1). Furthermore, the following five departments are below the national average with DTP3: Artibonite (64.8%), North (68%), South (74%), Northwest (65.3%) and Southwest (70.8%).

**Table 1:** Vaccine coverage in children < 1 year, Haiti 2008-2012

Year	BCG	Measles Rubella	DTP3	Polio3
2008	61	54 (a)	53	52
2009	66	60	68	65
2010	64	45	69	62
2011	82	58	85	79
2012	69	66 (b)	80	76

Source: Country report to PAHO (JRF)

(a) 2007 figure for the measles vaccine

(b) The country conducted a follow-up on children < 9 years of age, achieving >95% national coverage.

In this regard, the EPI has proposed 4 strategic lines of action for the purpose of improving access to vaccination services at the local level, achieving timely vaccination of the target population; these lines of action are the following:



- Reorganization of the network of vaccination services.
- Organization of vaccination services through the implementation of model immunization clinics. To date, 22 immunization clinics have been installed in each of the country's departments, including the Metropolitan Area, and the installation of at least 2 more per department is expected by the end of 2013.
- Definition of the best tactics for capturing the target population, according to the area of influence, demographics, population density and sociocultural characteristics.
- Integration of vaccination with other health interventions (such as vitamin A and deworming drugs).

As part of the improved access to vaccination services, the EPI has prioritized training on micro-planning at the local level, which includes the communication and social mobilization component. Likewise, in light of the weaknesses of the National Vaccination Program, training workshops have been held at the departmental level to improve the gathering and analysis of vaccination data. Timely supervision by department carried out by local professionals trained by PAHO will facilitate regular submission of high-quality data from the departmental level to the national level, achieving the indicators. Lastly, the EPI has obtained strategic partners' commitment to improve vaccine storage capacity immediately at the departmental level and in outlying areas. This is critical for timely introduction of the rotavirus vaccine (scheduled for the second semester) and the pneumococcal vaccine (2014).

#### *Epidemiological surveillance*

As part of the process for documenting and verifying the elimination of measles and rubella, the country demonstrated the absence of circulation of these viruses through the implementation of active searches in healthcare and community services during 2012. Similarly, the country carried out a retrospective search for congenital rubella syndrome (CRS) in selected institutions for the period 2007-2012, the results of which were zero cases of CRS detected.

Achievement of the indicators of the measles/rubella surveillance system has improved substantially since 2012. By epidemiological week (EW) 22/2013, the country had reported 124 suspected cases of measles and rubella, and had complied satisfactorily (>80%) with every surveillance indicator.

Surveillance of acute flaccid paralysis (AFP)/polio, tetanus and neonatal tetanus (NNT) continues to present significant challenges with regard to both periodic reporting of cases and compliance with indicators. In the case of polio, by EW 23, the notification rate for AFP was 0-17% per 100,000 <15 years of age and the percentage of adequate samples was 66%. Between 2009 and 2012, the country was in epidemiological silence for reporting cases of NNT. However, as part of the plan to eliminate neonatal tetanus, 65 at-risk municipalities were identified. In 2013, with support from Brazilian epidemiologists in each department, 2 cases of NNT were confirmed and investigated.



## RECOMMENDATIONS

- The TAG congratulates Haiti on the commendable progress made, and urges the national authorities to maintain their strong commitment to the regular immunization program.
- The country should, based on the strategic lines of action, prepare a road map to strengthen the regular immunization program. The implementation of this road map implies the development of a single plan of action agreed upon with the strategic partners, in order to guarantee timely mobilization of resources.
- The country should continue building national vaccination capacity, giving local professionals greater stability, for which the strategic partners should maintain ongoing support on the training and supervision of these professionals.
- The TAG endorses the ICE's specific recommendations for Haiti on the verification of the elimination of measles, rubella and CRS.
- The TAG urges Haiti to maintain its momentum in completing the agenda and facing new challenges in vaccination, such as the introduction of new vaccines.
- The country should formulate a communication and social mobilization plan aimed at generating a higher demand for vaccination.



## UPDATE ON THE STATUS OF PAHO'S REVOLVING FUND FOR VACCINE PROCUREMENT AND PROGRESS REPORT ON REGIONAL DEVELOPMENT OF VACCINES AND HEMODERIVATIVES

### *Status of the Revolving Fund*

For over 32 years, PAHO's Revolving Fund for vaccine procurement (RF) has been the strategic tool of countries in the Region, in order to gain access to a continuous, timely supply of good-quality vaccines at the lowest available price. During the meeting, key figures regarding the operation of the RF were presented and the context in which the RF operates and the importance of the countries' participation were explained.

In 2012, the RF purchased 60 products including 28 different biologicals on behalf of 34 countries and 7 territories. A total of 180 million doses were procured for a total purchase value of US\$512 million. The RF coordinated and monitored a total of 1200 shipments, arranging for their timely arrival. In that same year, the capital fund, which allows countries to reimburse PAHO for the purchase cost 60 days after the arrival of their orders, amounted to US\$102 million dollars. This is the result of the solidarity contribution of 3% over the countries' purchase value. More than 80% of the purchases were made using the line of credit, which to date amounts to US\$9 million for each country.

Its mission has not only contributed to the elimination of vaccine-preventable diseases, but also to quick and sustained introduction of new vaccines, as well as the financial self-sustainability of immunization programs in the Region. The continuous success of its mission mainly depends on three factors: the context of the global vaccine market, PAHO's role in the management of the mechanism, and countries' active, committed participation.

Currently, the global vaccine market poses challenges with regard to covering the Region's total demand and obtaining lower prices. There is a limited supply of vaccines, such as yellow fever, oral polio and acellular pertussis containing vaccines, to meet the global demand. In addition, limited competition in the supply of new vaccines (i.e. pneumococcal conjugate, rotavirus, human papillomavirus), plus the existence of other actors in the market, make providing access at even lower prices a challenge. The RF constantly seeks ways to meet the challenges found in the global vaccine context, while preserving its principles of Pan-Americanism, equity, universal access and quality.

Another challenge the RF has faced is related to the seasonal influenza vaccine. The RF has facilitated countries' access to it; however, the content of the inserts of some of the producers does not clearly indicate the use of the vaccine in recommended populations, such as pregnant women. In addition, given that, in the case of some producers, the same vaccine does not cover all of a country's target populations, from children to adults, awarding the bids according to countries' programmatic needs, ensuring competition among producers, has been a challenge.

With regard to the management of the RF, its Working Group, composed of representatives of PAHO technical and management areas, analyzes, recommends and implements policies, processes and tools for continuous improvement of the RF's performance. A planning tool for improved demand and the implementation of management monitoring systems that facilitate



monitoring the timely arrival of orders and the use of the capital fund, for example, are some of the improvements. In order to meet the challenges of the global vaccine market, long-term purchase agreements have been established and communication with the producers has been increased. In addition, coordination with other partners, such as the GAVI Alliance and UNICEF, is being improved in situations where the global supply is limited.

Once more, emphasis is placed on the fact that in order to maintain and strengthen the economy of scale and benefits of the RF, active and committed participation of countries and territories is important. Their commitment to oversee increasingly precise forecasts of demand, as well as timely payment of obligations, contributes to producers' trust in the RF. Changes in demand or cancellations on the part of countries mean that the producers assume opportunity costs, which affects the credibility of the RF with them and the supply in terms of quantity and price for everyone. In addition, requirements that were not planned originally are lost opportunities with regard to obtaining lower prices and are a challenge to the timely deliveries, as producers may not have the stock readily available.

### ***Progress Report: Developing regional vaccine and hemoderivative manufacturing capacity***

Some Latin America and the Caribbean countries have an important manufacturing capacity for vaccines and blood derived products. This capacity could potentially lead to the further development of a regional capacity. Following TAG recommendation of October 2012, PAHO held a workshop bringing together regionally-based vaccine manufacturers, national authorities from the ministries of health and the national regulatory authorities and other relevant stakeholders with the aim of strengthening this Regional capacity.

*The objectives of this workshop were:*

- establish a network to facilitate information sharing and actively cooperate in strengthening initiatives;
- identify political, financial, expertise and regulatory hurdles, and
- explore suitable mechanisms to determine medium and long-term vaccine demand.

*Meeting participants agreed on the following list of recommendations:*

- strengthen regional capacity to forecast and quantify future demands to better inform manufacturing decisions;
- facilitate and maintain an ongoing dialogue with other similar initiatives at the global and regional level, and, taking advantage of PAHO's leadership, enable discussions between different actors to meet any challenges that may emerge;
- PAHO, manufacturers and national authorities should map the current needs for production and innovation on vaccine and blood derivative to better inform the manufacturing decisions and to develop regional RD&I agendas for these products;



- ensure that technology transfer agreements respond to regional needs and have don't negative effects on the overall access to health technologies due to market segmentation; and
- taking into account the capacity of regulatory agencies in the Region, PAHO should explore viable alternatives to expand eligibility of vaccines to expand the supply of and access to additional vaccines and hemoderivatives, while ensuring quality requirements.

The development of a regional network that can share knowledge, information and other resources and advocate for necessary changes was identified as the foundation for the overall program of work. Regional National Regulatory Authorities (NRAs) play a fundamental role in ensuring the safety and quality of the products and facilitate their introduction into the health systems. Thus, the proposed regional network and eventual work plan should include a strong regulatory component and close coordination with Regional NRAs.

*Based on these general recommendations, participants agreed on the following next steps:*

- develop a Community of Practice within PRAIS to bring together regional manufacturers, national health and regulatory authorities and other relevant stakeholders, under PAHO's supervision, to improve coordination and communication towards improving access of vaccines and blood derivatives in the Region;
- map the current strengths, opportunity and needs on the supply of vaccines and blood derivatives. PAHO will circulate a survey among regional manufacturers to collect the necessary information;
- coordinate and link with other relevant initiatives and networks and look for synergies at the regional and global levels; and
- develop network bylaws, once the survey information is systematized, functionally and structure and work plan that can guide the activities of the network. The proposal should be holistic and encompass technical, political and financial components. The initiative needs to ensure funds to implement any work plan.

## RECOMMENDATIONS

- TAG reiterates its recognition of the RF as a key pillar of immunization programs and reconfirms its recommendations<sup>3</sup> made in October 2012 on the importance of countries' ongoing participation, and that PAHO maintain communication and coordination with the main partners in the global field of immunization, in order to take advantage of opportunities and meet the challenges of the global vaccine market.

<sup>3</sup> TAG Report, October 2012, page 19

[http://new.paho.org/hq/index.php?option=com\\_docman&task=doc\\_download&gid=19264&Itemid=270&lang=es](http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=19264&Itemid=270&lang=es)



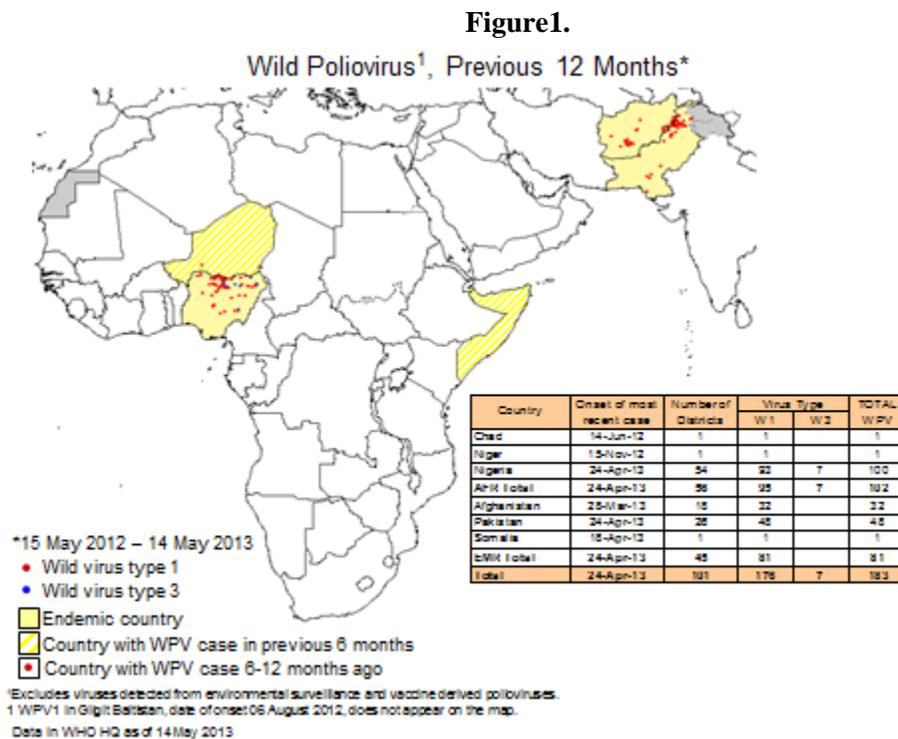
- TAG recommends that countries ensure more accurate demand forecasts. The Revolving Fund should provide the countries with support on the planning and follow-up process.
- PAHO should continue with its commitment to strengthen operating and financial management of the Revolving Fund in order to provide increasingly better service and greater capacity to extend credit to participating countries and territories.
- The TAG ratifies the importance of developing regional vaccine production capacity as a strategy to strengthen implementation of immunization and health programs in the region. PAHO should continue to lead the network and its work program. It also calls for the producers, regulatory agencies, health authorities and actors maintain an active interest in the work program as soon as it is established.



## POLIO

The last endemic wild poliovirus was detected in the Region of the Americas in 1991, and in 1994 the International Commission for the Certification of Poliomyelitis Eradication (ICCP), established by PAHO's director, certified the Region of the Americas to be polio-free. Since its elimination in 1991, the Region has not have outbreak due to importations of wild polio viruses, and the only cVDPV outbreak occurred in 2000-2001 in the Dominican Republic and Haiti, and was caused by a type 1 polio-derived virus. The elimination was achieved using tOPV and the TAG recommended the OPV as the vaccine of choice for the American Region as long as wild poliovirus continues to circulate in the world.

The progress towards global polio eradication continues, and by the end of 2012, the total number of polio cases worldwide decreased 66% over the previous year to 223.



Wild poliovirus (WPV) was endemic only in Afghanistan, Nigeria and Pakistan, and three of the four countries that had re-established WPV transmission following importations (Angola, the Democratic Republic of the Congo and Sudan) did not have a single case in 2012. The fourth, Chad, has not reported a case since June 2012.

On May 2012, the World Health Assembly declared ending polio a “programmatically emergency for global public health” and called on the WHO’s Director-General to develop and finalize a comprehensive polio endgame strategy. The Polio Eradication and Endgame Strategic



Plan 2013-2018 was developed to capitalize on this new opportunity to end all polio disease. It accounts for the parallel pursuit of wild poliovirus eradication and circulating vaccine-derived poliovirus (cVDPV) elimination, while planning for the backbone of the polio effort to be used for delivering other health services to the world's most vulnerable children.

The Plan has four major objectives. The first one is to stop all wild poliovirus transmission by the end of 2014 and any new outbreaks due to cVDPV within 120 days of confirmation of the index case. The second objective is Immunization system strengthening and OPV withdrawal. This objective engages all 144 countries that currently use OPV and calls for the withdrawal of the type 2 component from the trivalent OPV and the introduction of at least one dose of affordable IPV (inactivated polio vaccine). Objective number three is to certify all of the regions of the world as polio free and ensure that all poliovirus reserves are safely confined. Finally, objective number four is Legacy Planning.

In 2012, the SAGE, the world's chief policy guidance body for immunization, recommended the withdrawal of the type 2 component of oral polio vaccine (OPV) as soon as possible from routine immunization programmes<sup>1</sup> in all countries, facilitated by the introduction of at least one dose of IPV. In April 2013, the Scientific Community endorsed the Plan. The SAGE recommendation is based on the fact that "poliovirus type 2 was eliminated in 1999 and that the continued use of trivalent Oral Polio Vaccine (tOPV), in areas where coverage is not adequate, contributes to ongoing type 2 vaccine-associated paralytic poliomyelitis and vaccine-derived virus outbreaks (cVDPV)" The SAGE working group emphasized that before interrupting the use of the type 2 vaccine, the following conditions should be met: the current outbreak of cVDPV2 in Nigeria must be interrupted; absence of outbreaks caused by cVDPV2 for at least one year; adequate epidemiological surveillance that makes it possible to detect and control any cVDPV2 outbreak; adequate quantities of bOPV available; an inactivated polio vaccine (IPV) at an affordable price, a global reserve of type 2 monovalent vaccine (mOPV); and an international agreement to discontinue the global use of tOPV.

In April 2013, the by members of the scientific community signed the Scientific Declaration on Polio Eradication, which endorses the Eradication and Endgame Strategic Plan and called on actors in the global community to do their part to ensure the full implementation of the plan.

During this meeting the TAG received a report on the global eradication situation, the scenarios for polio vaccine supply, the status of the epidemiological surveillance in the Americas and on the Polio Eradication and Endgame Strategic Plan 2013-2018. The TAG discussed the implication of a potential change in vaccination recommendations and noted that the Region eliminated polio and has remained polio-free using the tOPV.

## RECOMMENDATIONS

- Countries of the Americas must wait for the fulfillment of the conditions stated by SAGE for the cessation of the use of Sabin type 2 containing vaccines; these conditions must be met before making any change in vaccination policy. As long as there are outbreaks caused by cVDPV type 2 and the wild poliovirus continues to circulate in the world, the trivalent oral polio vaccine (tOPV) remains the vaccine of choice for the Americas.



- PAHO should convene a Working Group to develop a strategic plan describing current options and scenarios, as well as the timelines for the implementation of the polio endgame in the Americas. This plan should discuss the feasibility of using different OPV/IPV schedules; the availability of combination vaccines containing IPV, where the ideal situation would be having an hexavalent DTwP-Hib-IPV-HepB vaccine, among other issues.
- All countries must reinforce the activities aimed to achieve or maintain vaccination coverage >95% in every district or municipality. If countries do not achieve that coverage they must evaluate the accumulation of non-immunized and conduct vaccination campaigns.
- All countries must continue to maintain adequate acute flaccid paralysis (AFP) surveillance in order to timely detect any importation or emergence of VDPVs, and must report to PAHO on a timely fashion to allow the proper monitoring of the Regional situation.
- TAG reinforces its previous recommendations (Argentina 2011) for countries considering the introduction of inactivated polio vaccine (IPV): compliance with sanitary conditions and vaccination coverage guaranteeing an adequate protection to their communities.
- PAHO must continue to maintain a dialogue with vaccine suppliers in order to guarantee the provision of polio vaccines for the Americas.



## MONITORING AND REPORTING OF GVAP INDICATORS

The Global Vaccine Action Plan (GVAP) is an effort to strengthen the achievements of immunization and continue urging governments to continue with their commitment to protect their populations from vaccine-preventable diseases. The GVAP builds on the Global Immunization Vision and Strategy (GIVS), which was launched in 2005 and was the first 10-year strategic framework to maximize the potential of immunization. The GVAP reiterates the existing global goals and proposes new goals for this Decade of Vaccines (2010-2020). On May 25, 2012, in its 65th meeting, the World Health Assembly backed the GVAP and passed Resolution 65.17 on behalf of this plan. A year later, WHO and its partners have made progress on the definition of a Monitoring and Accountability Framework for the purpose of documenting the GVAP's impact. This monitoring framework will be adapted to the needs of the programs in the 6 different regions and 194 member countries of the WHO.

In the Americas, the GVAP will complement the Regional Immunization Vision and Strategy, a document that was developed to adapt the GIVS to regional priorities in 2007. The monitoring and reporting mechanisms for measuring the Region's progress regarding the GIVS will be used to monitor the implementation of the GVAP.

The GVAP has indicators, with targets for 2015 and 2020, to track progress on the 5 goals of the plan (Table 1) and 16 indicators to track progress on the plan's 6 strategic lines of action (Table 2). The Monitoring and Accountability Framework establishes data gathering for these indicators as a shared responsibility of the different levels of the immunization community: the global, regional and national levels. The majority of these monitoring indicators are based on information that is gathered routinely in this Region, with the exception of vaccination coverage reported by income level (Table 2) and the evaluation of the degree of confidence in vaccines among the population. Special studies should complement the WHO/UNICEF Joint Reporting Form (JRF), which will be the primary reporting mechanism for GVAP monitoring.

The reporting of these indicators will be a shared responsibility between the national, regional and global levels. All proposed indicators with the exception of those related to strategic objective 6, which monitors progress in research and development of new vaccines, require information from the national level. WHO will gather data and monitor progress on strategic objective 6 at the global level. Through the JRF, Member States will continue reporting to PAHO on the technical and programmatic performance of the national immunization programs (NIP) in March of each year. In preparation for submission of the JRF, the NIP should begin the process of analyzing data at the beginning of each year, reviewing national data with the partners of the NIP (interagency committees) and with national immunization technical advisory groups (NITAGs) where they exist. This review will serve to adapt GVAP monitoring at the national level and disseminate progress regarding the goals with the actors involved in the NIP. After finalizing the national process of gathering, synthesizing and disseminating the annual EPI progress, PAHO will consolidate this information and share it with the Regional Technical Advisory Group (Regional TAG), the PAHO Directing Council and WHO.



## RECOMMENDATIONS

- TAG applauds the Member States for joining global efforts to extend the benefits of immunization to all individuals during this Decade of Vaccines (2010-2020) through the GVAP.
- TAG recognizes the efforts of the Member States in monitoring progress towards achieving the national and regional immunization goals and encourages the NIPs to continue to provide timely reporting of progress to PAHO through the WHO-UNICEF JRF.
- PAHO should, in the context of GVAP, report annual progress to the organization's Governing Bodies, the TAG and WHO.



**Table 1: Indicators for global level goals**

Goal	Target by 2015	Target by 2020
1) Achieve a world free of poliomyelitis	<b>1) Interrupt wild poliovirus transmission globally (by 2014)</b>	<b>1) Certification of poliomyelitis eradication (by 2018)</b>
2) Meet global and regional elimination targets	<b>2a) Neonatal tetanus eliminated in all WHO regions 2b) Measles eliminated in at least four WHO regions 2c) Rubella/congenital rubella syndrome eliminated in at least two WHO regions</b>	<b>2) Measles and rubella eliminated in at least five WHO regions</b>
2) Meet vaccination coverage targets in every region, country and community	<b>3) Reach 90% national coverage and 80% in every district or equivalent administrative unit with vaccines containing diphtheria-tetanus pertussis</b>	<b>3) Reach 90% national coverage and 80% in every district or equivalent administrative unit with all vaccines in national programmes, unless otherwise recommended</b>
4) Develop and introduce new and improved vaccines and technologies	<b>4) At least 90 low- and middle-income countries have introduced one or more new or underutilized vaccines</b>	<b>4a) All low- and middle-income countries have introduced one or more new or underutilized vaccines 4b) Licensure and launch of vaccine or vaccines against one or more major currently non-vaccine preventable diseases 4c) Licensure and launch of at least one platform delivery technology</b>
5) Exceed the Millennium Development Goal 4 target for reducing child mortality	<b>5a) Reduce by two thirds, between 1990 and 2015, the under-five mortality rate (Target 4.A)</b>	<b>5a) Exceed the Millennium Development Goal 4 Target 4.A for reducing child mortality</b>

\*Indicators in bold fall under the responsibility of the national/regional level.



**Table 2: Indicators for strategic objectives**

Objetivo estratégico	Indicadores
1) All countries commit themselves to immunization as a priority	<ul style="list-style-type: none"> <li>• Domestic expenditures per person targeted</li> <li>• Presence of an independent technical advisory group that meets defined criteria</li> </ul>
2) Individuals and communities understand the value of vaccines and demand immunization both as a right and a responsibility	<ul style="list-style-type: none"> <li>• Percentage of countries that have assessed (or measured) confidence in vaccination at subnational level<sup>1</sup></li> <li>• Percentage of unvaccinated and under-vaccinated people in whom lack of confidence was a factor that influenced their decision</li> </ul>
3) The benefits of immunization are equitably extended to all people	<ul style="list-style-type: none"> <li>• Percentage of districts with 80% or greater coverage with three doses of diphtheria-tetanus-pertussis-containing vaccine</li> <li>• Reduction in coverage gaps between lowest and highest wealth quintile and another appropriate equity indicator</li> </ul>
4) Strong immunization systems are an integral part of a well-functioning health system	<ul style="list-style-type: none"> <li>• Dropout rate between first dose and third dose of diphtheria-tetanus-pertussis-containing vaccines</li> <li>• Sustained coverage with diphtheria-tetanus-pertussis containing vaccines of 90% for three or more years</li> <li>• Immunization coverage data assessed as high quality by WHO and UNICEF</li> <li>• Number of countries with case-based surveillance for vaccine-preventable diseases that meets quality standards</li> </ul>
5) Immunization programmes have sustainable access to predictable funding, quality supply and innovative technologies <sup>2</sup>	<ul style="list-style-type: none"> <li>• Percentage of doses of vaccine used worldwide that are of assured quality</li> </ul>
6) Country, regional and global research and development innovations maximize the benefits of immunization	<ul style="list-style-type: none"> <li>• Progress towards development of vaccines against HIV infection, tuberculosis and malaria</li> <li>• Progress towards a universal influenza vaccine (protecting against drift and shift variants)</li> <li>• Progress towards institutional and technical capacity for conducting vaccine clinical trials</li> <li>• Number of vaccines that have either been re-licensed or licensed for use in a controlled-temperature chain at temperatures above the traditional 2–8 °C range</li> <li>• Number of vaccine-delivery technologies (devices and equipment) that have received WHO prequalification compared to 2010</li> </ul>

\*Indicators in bold fall under the responsibility of the national/regional level.



## MENINGOCOCCAL DISEASE AND VACCINES CURRENTLY AVAILABLE

Meningococcal disease (MD) refers to the spectrum of infections caused by *Neisseria meningitides* including meningitis, bacteremia and bacteremic pneumonia. In the majority of countries, *Neisseria meningitides* is recognized as the leading cause of fulminant meningitis and *septicaemia*. Therefore, it is considered to be a significant public health problem. MD is associated with high mortality (10-20%), and approximately 20% of survivors develop sequelae, such as deafness, neurological deficit or amputation of a limb.

MD affects every age group, but the highest incidences are found in children under five, especially those under one year of age. In some populations, peaks of incidence may also occur in adolescents or young adults and adults over 65 years of age. During outbreaks and epidemics, changes tend to occur where the highest incidence rates are in adolescents and young adults. The majority of MD cases are sporadic. The disease presents seasonal variations, especially in the winter, and outbreaks occur at irregular intervals. Invasive meningococcal infections are mainly caused by serogroups A, B, C, X, W135 or Y capsular polysaccharides, but is important to note that this disease is marked by great variation in relation with the distribution of serogroups by region and over time.

*Neisseria meningitides* has become the leading cause of bacterial meningitis in children in Latin America and the Caribbean, especially, following the introduction of the *Haemophilus influenzae* type b vaccine in routine vaccination schedules. In Latin America and the Caribbean, the incidence of MD varies widely, with rates ranging from <0.1 cases per 100,000 inhabitants in countries such as Mexico, to 2 cases per 100,000 inhabitants in Brazil.

Although MD is a notifiable disease, its incidence in the majority of countries in the Region is likely underestimated, since in many countries the epidemiological surveillance systems for this disease are weak and the information available is of poor quality. When data from the different countries are analyzed, problems detected include considerable heterogeneity in the quality of the information; significant variability in morbidity and mortality records; very low rates of incidence as a consequence of under-registration; and a large proportion of meningitis cases without an identified etiological agent, due to limitations in obtaining adequate specimens for culture and prior use of antibiotics.

In Latin America, available data indicate that serogroups B and C are still responsible for the majority of cases. Serogroups W135 and Y are emerging and have been reported in some countries, while serogroup A has virtually disappeared in the Region. Although the proportion of isolated serotypes in the Region is known, the burden of disease cannot be inferred from these serotypes due to the aforementioned weaknesses in epidemiological surveillance.

There are single meningococcal polysaccharide vaccines or vaccines conjugated with a carrier protein. Although polysaccharide vaccines produce an antibody response, conjugate vaccines are more immunogenic and also induce immunological memory. Polysaccharide and conjugate vaccines against meningococcal groups A, C, W135 and Y are available in the market. Both vaccines are safe and effective. The polysaccharide vaccine does not provide adequate immunity in children aged <2 years of age and in children over 2 years of age, it offers limited-duration



immunity because it does not induce immunological memory. Recently, in January 2013, the first recombinant meningococcal serogroup B vaccine was licensed by the European Commission.

## RECOMMENDATIONS

- It is imperative that the countries implement systems for epidemiological surveillance of meningococcal disease in order to know its real magnitude and epidemiological profile. PAHO should continue providing guidance for the standardization of lab diagnostic methods and for the reporting of the disease.
- Countries that already have sentinel epidemiological surveillance for bacterial meningitis and pneumonia in children under five should establish a plan of action to improve the quality of information, including improvement in and standardization of diagnostic laboratory techniques.
- Countries should establish sentinel sites for other age groups for bacterial meningitis and pneumonia, using standard laboratory techniques and case definitions.
- Countries should analyze their epidemiology, during outbreaks and epidemics, before making decisions regarding control measures, including the identification of groups to vaccinate and the vaccine to be used.
- Countries with high burden of disease in young children that decide to introduce meningococcal conjugate vaccine as part of the routine immunization program targeting children aged <1 or <2 years should ideally include catch-up vaccination of children and adolescents, or at least of adolescents, given that this is the age-group with the highest carriage levels.



## PROGRESS IN THE INTEGRATION OF EPI COSTING AND PLANNING

If we compare the situation of the Expanded Program on Immunization (EPI) in the year in which it was created (1974) with the current situation, we find that:

- Early on, the EPI had vaccines against 6 diseases (tuberculosis, polio, diphtheria, pertussis, tetanus and measles) available. It currently protects against 14 diseases (including hepatitis b, *Haemophilus influenzae* type b, rubella, mumps, pneumococcal disease, rotavirus, yellow fever, influenza and human papilloma virus).
- The EPI used to administer a total of 10 doses per child, while currently it delivers up to 20 doses per child.
- The EPI used to vaccinate children exclusively, while it now vaccinates entire families. Today, adolescents, pregnant women, occupational risk groups and the elderly receive vaccines.
- The annual cohort to vaccinate in the Region in 1975 was approximately five million children under 1 year of age, while for 2011 the cohort comprised nearly 15 million children less than one year of age.
- The cost per child vaccinated was less than five dollars then, while it is currently approximately 70 dollars per child immunized, taking into account only the cost of the vaccines.

Given the above considerations, planning and costing for the EPI requires careful work based on data for adequate decision-making and to ensure the program's sustainability.

In 1974, with the creation of the EPI, an annual planning tool was generated that included nine areas of action or components of the plan of action (Biologicals and supplies, Cold chain, Training, Social mobilization, Operating expenses, Supervision, Epidemiological surveillance, Research and Evaluation). Due to the rapid development of the program, countries independently introduced other required components according to their scope of work (i.e. management, coordination, logistics, new vaccines, etc.). Thus, countries currently send PAHO their plans of action with a variable number of EPI components, and they include different activities in one component or another according to their own criteria. At the same time, PAHP requests that countries submit separate plans for certain activities (such as campaigns) that are not included in the master plan of action. This makes it difficult to compare across different country plans or to adequately interpret each plan, since it is not clear which activities have been included in each component. For all of these reasons, PAHO has proposed the standardization of all of the existing tools (Plan of Action form, WHO-UNICEF Joint Reporting Form, multi-year immunization plans and the GAVI report, among others) through the creation of a standard definition of the 12 components of the EPI and their content.



Countries in the Region consistently carry out a planning process based on: 1) national government and, specifically, health sector planning, 2) the reality in the country 3) the teams' technical capacity 4) the team's participation, as well as that of other actors involved in the process, 5) monitoring and evaluation allows for the adaptation of activities, and 6) a defined budget framework. This systematic process has contributed to strengthening EPI management and the mobilization of resources for the EPI. However, greater integration is still required in order to avoid duplicative efforts and to facilitate the management and monitoring of the plan's execution.

In addition, it is important to perform adequate costing of past activities periodically, in order to provide greater clarity on details of budget execution. This facilitates better understanding of the components and activities that consume the greatest amount of resources, as well as the identification of inefficiencies and opportunities for improvement in the operational and logistic aspects of the EPI.

Currently, the majority of countries do not routinely perform costing studies at every level of the EPI; nor do they have a methodology or tool to perform these studies adequately, which requires gathering information on costs and resource use through adequate sampling of healthcare facilities throughout the country. The ProVac initiative has developed a tool and methodology called CostVac, which is a package of materials designed so that EPI coordinators can select an adequate sample of vaccination centers, adapt surveys to the national situation and analyze the information gathered within a standard, consistent framework. In 2012 and 2013, a pilot study was conducted on EPI costing in Honduras using the CostVac tool and methodology. For the first time, the Honduran EPI gathered information on costs and the use of resources at the local level at 71 health facilities in 8 of the country's regions. The information gathered from the healthcare facilities and regional offices showed that over 50 percent of the economic costs of the EPI are incurred at the healthcare facility level. These costs are generally underestimated at the central level, and taking them into account can help in distributing limited resources more efficiently. In addition, a more precise estimate of the real cost of the EPI will serve as an important input for management of the EPI and mobilization of resources.

PAHO has proposed a tool for integrating planning and costing of the program that countries can use to produce simpler costing information annually, which will be useful for the planning and budgeting of the following year. They will also be able to do more thorough five-year costing (accompanied by an international evaluation of the EPI or independently) for the purpose of performing closer analysis of the efficiency of the program and identifying challenges and opportunities for improvement. The information on cost of immunization should be complemented with information regarding the benefit provided by the program, such as prevention of disease and therefore reduction of costs regarding hospitalization, treatment, rehabilitation services, days-off and immeasurable suffer and sorrow. The cost of immunization should always be compared with its absence. Therefore, it should be considered a sound investment and not costs because health is essential for economic development.

## RECOMMENDATIONS

- Recognizing that costing of the EPI is of great value for making informed decisions when planning immunization activities and negotiating the budget; countries should test and adopt the tools proposed by PAHO.



## VACCINATION WEEK IN THE AMERICAS

In April 2013, Vaccination Week in the Americas (VWA) was celebrated for the eleventh time. Over its tenure in the Region, more than 450 million individuals have been vaccinated under the framework of the initiative. VWA has also become a key annual opportunity to promote equity and access to vaccination services and to highlight the work of national programs through the media. The regional slogan for VWA 2013 was “Vaccination: a shared responsibility,” which was chosen to highlight the importance of governments, health care workers, parents and children each doing their part to support national immunization programs and maintain high coverage. VWA 2013 was covered by press outlets in more than 29 countries in the Region, in addition to information disseminated by other agencies and partners (such as UNICEF, United Nations Information Centre, GAVI and the Bill and Melinda Gates Foundation).

Dozens of national and international launching events were carried out to celebrate VWA 2013. Two regional launches were held with the participation of PAHO’s Director, Dr. Carissa F. Etienne. The first regional launch took place on 24 April in the adjacency zone between Benque Viejo, Belize, and Melchor de Mencos, Guatemala and served as a bridge to peace, reinforcing diplomacy and confidence between both nations, a process supported by the Organization of American States. The second regional launch was held on 27 April in Carrefour, Haiti, outside of Port-au-Prince. These events counted on the participation of high level authorities including Ministers of Health, partner organizations such as GAVI and the United States Centers for Disease Control and Prevention (CDC), and other United Nations Agencies (UN), such as UNICEF, UNAIDS and UNOPS, and the UN Resident Coordinators of Belize and Haiti, who participated on behalf of the Secretary- General.

Based on country VWA plans and reports submitted to PAHO headquarters, to date, 44 countries and territories participated in VWA 2013, targeting approximately 44 million people for vaccination against diseases including poliomyelitis, measles, mumps, rubella, and congenital rubella syndrome, diphtheria, whooping cough, tetanus, hepatitis B, seasonal influenza, yellow fever, diarrhea caused by rotavirus and bacterial pneumonia, in a wide variety of campaigns. Of note, several countries carried out immunization or promotional campaigns focused on the human papillomavirus (HPV) vaccine this year. Eighteen countries and territories also integrated other preventative interventions with vaccination, including deworming, vitamin A supplementation, growth monitoring, cancer detection and health screenings, among others.

This year also marked the second celebration of World Immunization Week (WIW), which was endorsed by the World Health Assembly in 2012 following a global movement of sister initiatives being established in all other regions of the WHO and advocacy efforts on the part of Member States. The slogan for WIW was “Protect your world, get vaccinated” and overarching activities were coordinated by the WHO headquarters office. In 2013, the themes for vaccination week initiatives around the world included:



- 8th European Immunization Week-“Prevent. Protect. Immunize.”
- 4th Vaccination Week in the Eastern Mediterranean-“Stop Measles Now!”
- 3rd African Vaccination Week-“Prevent disabilities, vaccinate!”
- 3rd Vaccination Week in the Western Pacific-“Finish the job-No more measles for anyone”
- 2nd Vaccination Week in South-East Asia focused on the intensification of routine immunization

## RECOMMENDATIONS

- TAG congratulates all countries and territories in the Region for their exemplary achievements over the history of VWA and for the establishment of World Immunization Week.
- VWA should continue to be supported as an initiative that strengthens routine vaccination programs in the Region and helps to ensure political commitment to them.
- The use of VWA as a platform for the integration of other preventative interventions should be continued in countries where it is applicable, and countries should also continue to explore methodologies to evaluate VWA’s impact on the routine program.



**Vaccinations in Disaster Situations:  
Recommendations from the PAHO/WHO – Comprehensive Family Immunization Unit,  
Department of Family Health, Gender and Life Course (IM/FGL)**

- 1) Ensure that all displaced people and/or people in shelters (adults and children), including health workers in the shelters and international humanitarian responders (such as personnel of international organizations, philanthropic church members), are vaccinated against measles/rubella and polio.
- 2) Attempt to maintain routine vaccination with the basic vaccination schedule, since a reduction in coverage in the medium-term could result in a resurgence of vaccine-preventable diseases that have already been controlled and/or eradicated, such as measles, rubella, polio, whooping cough, diphtheria, and tetanus.
- 3) Evaluate damage to the cold chain and the loss of biologicals and supplies (syringes).
- 4) Implement the temporary use of cold boxes to ensure the conservation of vaccines in the affected areas and their distribution, provided that there is ice available.
- 5) Implement the use of photovoltaic refrigerators for vaccine storage and ice production, guaranteeing sufficient batteries.
- 6) Initiate recovery of the cold chain (purchase of refrigerators, thermos, thermometers)
- 7) If cold chain allows it, immediately re-stock vaccines utilized routinely by national immunization programs.

Conditions during disasters and humanitarian emergencies favor an increase in the incidence of diarrheal diseases (associated with sanitation and water quality) and respiratory diseases (overcrowding). As part of an initial needs assessment, immunization activities (especially, vaccination with measles-rubella containing vaccine) should be evaluated along with other emergency health interventions. Generally, mass immunization during situations of natural disasters is not indicated and could divert limited human resources and materials from other more effective and urgent measures. Immunization campaigns could give a false sense of security, leading to the neglect of basic measures of hygiene and sanitation, which are more important during the emergency. Also, campaigns under difficult situations are not exempt from risks. However, when warranted, vaccination activities can save lives.

Mass vaccination would be justified when the recommended sanitary measures do not have an effect and if there is evidence of the progressive increase in the number of cases with the risk of an epidemic.



PAHO recommends that country health official and partner humanitarian agencies follow the three steps proposed by the Framework for Decision-making for Vaccination in Acute Humanitarian Emergencies, endorsed by the WHO's SAGE:

- 1) An assessment of the epidemiological risk posed by each potentially important vaccine-preventable disease within a given context;
- 2) A consideration of the properties of each vaccine to be considered for intervention; and
- 3) Prioritization of the importance of vaccination in relation to other urgent public health interventions, carefully considering key ethical principles and prevailing contextual factors.

In general, vaccines with the following characteristics could be considered useful in this situation:

- Vaccines of proven efficacy, high safety and low reactogenicity;
- Vaccines that are easy to apply (single-dose) and logistically feasible to maintain within the cold chain (storage available);
- Vaccines that confer rapid and long-lasting protection for people of all ages;
- Vaccines that are WHO prequalified, affordable, and that are available in sufficient quantities to guarantee the supply for the entire population at risk.

PAHO recommends that the use of these vaccines only be considered based on a careful assessment of pros and cons and under deliberation of the (potentially negative) operational, logistical and communication issues, following the steps described in the Framework.

Priority consideration would be given to vaccines currently used in national programs, especially the measles-rubella and polio vaccines to prevent the reintroduction of the viruses, yellow fever when urban spreading is possible, and tetanus toxoid- or tetanus-diphtheria vaccine early in the disaster to prevent tetanus cases after a mass injury event:

- **Measles and rubella:** measles is the most feared vaccine-preventable disease following a disaster or humanitarian emergency, given its high transmissibility and high case fatality rates among young, malnourished children, particularly in situations of overcrowding. Even though rubella is generally a mild disease, it can lead to Congenital Rubella Syndrome (CRS) when it affects pregnant women, particularly during the first trimester. The endemic transmission of both measles and rubella has been interrupted in the Western Hemisphere, therefore, when measles vaccination activities are conducted in the Region, measles and rubella-containing vaccines i.e., measles-rubella (MR) or measles-mumps-rubella (MMR), are used. Previous vaccination or history of disease are not contraindications to receive a measles-rubella-containing vaccine. The age group to be target will depend on a risk assessment and the analysis of cohorts previously vaccinated. To prevent the importation of measles or rubella to countries of the Americas, humanitarian assistant teams need to be vaccinated prior to arrival.



- **Polio:** The Americas has been free of wild poliovirus since 1991. In a disaster or emergency situation, the main threat is the reintroduction of poliovirus. The oral polio vaccine (OPV) is easy to administer and can be given concomitantly with other vaccines. As with measles/rubella, humanitarian assistance teams need to be vaccinated prior to arrival.
- **Yellow fever:** This mosquito-borne disease is endemic in tropical regions of South America. Vaccination should be considered if the risk of an outbreak is high, particularly if urban spread is possible. If the emergency situation is in an area considered enzootic for yellow fever, humanitarian assistance teams should be vaccinated prior to arrival.
- **Tetanus:** Increases in non-neonatal tetanus have been seen during the first 2-3 weeks following disasters that result in the injury of large numbers of people, such as earthquakes. The use of tetanus toxoid, in addition to the proper use of tetanus immune globulin, is important for proper wound management.

Regarding questions on the possible use and demand during an emergency for vaccines that are not included in national immunization programs, it is important to recognize the costs and mobilization efforts needed to carry out a mass immunization. The vaccines frequently proposed are those against cholera, typhoid fever, and meningococcal meningitis.

- **Cholera vaccine:** Two killed whole-cell vaccines are available on the global market and are WHO-prequalified. Both require a two-dose immunization series and concerns exist on the operational and logistic challenges associated to their outbreak and/or post-disaster deployment. Also, protection may only occur after 10 days of the series completion and only lasts for 2–3 years. Other effective and time-tested prevention and control measures exist for cholera outbreaks.
- **Typhoid fever vaccine:** Also given the progressively reduced effectiveness of antibiotics, new single-dose typhoid vaccines potentially open new opportunities for typhoid fever prevention and control. Experience on their deployment, for example in the vaccination of high burden and at risk populations, will tell about their benefits within a comprehensive approach that combines treatment, hygiene and sanitation. In the Americas, significant improvements in sanitation that occurred in the first half of the 1990s and related to the cholera epidemics were key to virtually eliminate typhoid fever from the continent.
- **Meningococcal vaccines:** These vaccines have been used to control meningococcal meningitis due to Groups A, C, W135 or Y in epidemic emergencies. Once epidemiological surveillance determines an increase in incidence and identifies the responsible serogroup, age group, and affected area or region, then vaccination can be considered. Two types of vaccines against meningococcal exist: polysaccharide vaccines and conjugate vaccines. The conjugate vaccines are used in routine vaccination programs, to protect people at high risk or in the case of outbreaks, according to the epidemiological situation, public health priorities, and the economic conditions of each country. Polysaccharide vaccines can be used to control outbreaks in countries where limited economic resources or insufficient supply restrict the use of meningococcal conjugate vaccines. In the case of serogroup A or C outbreaks, bivalent A, C polysaccharide vaccine is recommended for mass campaigns. However, due to the limited efficacy of polysaccharide vaccines in children <2 years of age, in confirmed group C



outbreaks MenC conjugate vaccines should be used for protection of those aged 2–24 months. Similarly, during group A outbreaks, MenA conjugate vaccine is the preferred option for protection of children 12–24 months of age. Meningococcal outbreaks caused by the W135 or Y serogroups require trivalent (A,C,W135) or quadrivalent (A,C,W135,Y) polysaccharide vaccines. The vaccination of close contacts in the case of outbreaks, depending on the availability of the vaccine against the specific serogroup, should coincide with the administration of the chemoprophylaxis. A stock of meningococcal vaccine should be established in order to ensure immediate availability for outbreak control if needed.

Other vaccines that are sometimes discussed include rotavirus, *Haemophilus influenzae* type b, pneumococcal vaccines, hepatitis A and B. Below is a summary of the vaccines in question:

- **Rotavirus vaccine:** Currently there are two available vaccines in the market, both prequalified by WHO. Field studies have demonstrated its effectiveness in preventing severe cases of gastroenteritis and an important reduction in hospitalizations due to rotavirus. Two or three oral vaccine doses are required, depending on the vaccine to be administered. At least one-month intervals should be provided between doses. The effectiveness of this vaccine has not been verified in emergencies.
- ***Haemophilus influenzae* type b vaccine:** This vaccine has had a significant impact on meningitis, pneumonia and other invasive forms of the disease, once introduced into routine immunization programs. The disease is not epidemic and as a result is not considered a problem in disaster situations. The disease occurs mostly in children under 2 years of age, and to induce protection at least 2 doses are required with a minimum interval of 1 month.
- **Pneumococcal vaccines:** Currently there are two types of pneumococcal vaccines available in the market: the polysaccharide vaccine with 23 serotypes (PPV23) and the 10 and 13 valent conjugate vaccines (PCV). The PPV23 vaccine is indicated for people aged 65 years or older and people with increased risk of invasive pneumococcal disease (carriers of asplenia, alcoholism, hematologic and other cancers, diabetes mellitus, chronic liver, cardiovascular, pulmonary and renal diseases, cerebrospinal fluid fistulas, hemoglobinopathies, acquired or congenital immunodeficiencies, organ or hematopoietic stem cell recipients and recipients of immunosuppressive therapy including systemic corticosteroids, and nephrotic syndrome). Usually a single dose is administered. Among children, the highest pneumococcal disease burden is borne by children aged <5 years. In the routine immunization program, PCV is usually recommended in a three-dose schedule for children aged <2 years. It is recommended that priority be given to children with increased risk of invasive pneumococcal disease as previously described. Both vaccines are relatively expensive and there are no studies regarding their application in disaster situations.
- **Hepatitis A vaccine:** Some areas are endemic for infection by hepatitis A virus and infection occurs at an early age. It is transmitted person to person or through food and polluted water, which means that a common source may lead to outbreaks. Pathogenicity varies with age and is more serious in adults. In children under 6 years, infection is often asymptomatic. Current hepatitis A vaccines are licensed for persons aged  $\geq 1$  year. According to the manufacturers, a complete vaccination schedule consists of 2 doses administered into the deltoid muscle. However, new evidence suggests that a single dose of this vaccine may successfully control



outbreaks of hepatitis A. Use of this vaccine in emergencies will depend on the analysis of risk and vaccine availability vis-à-vis the particular situation. Humanitarian assistant teams may consider this vaccine depending on the level of transmission in the affected area.

- **Hepatitis B vaccine:** Hepatitis B is not epidemic-prone, although clusters could occur following mass sexual violence events. Humanitarian assistant teams may consider this vaccine. In terms of disease burden, in the Americas, the highest prevalence area is the Amazon Basin.



**Meeting of the Vaccine-preventable Disease Laboratory Networks for the  
Region of the Americas  
Quito, Ecuador  
2 July 2013**

A meeting of the Regional of Vaccine-preventable Disease (VPD) Laboratory Networks was held in Quito, Ecuador on 2 July 2013. The purpose of this meeting was identifying the capacities, strengths and opportunities for maintaining the achievements, facing new challenges, and improving the performance of the Networks. The meeting was attended by 25 representatives from the Region's public health labs, technical experts from the Argentina's Malbran Institute and the US Centers for Disease Control and Prevention (CDC), as well as by PAHO national and regional immunization advisors.

The objectives of this meeting were to:

1. Review the progress of the Americas' Regional Networks of VPD Laboratories and discuss the possibility of a Network of VPD Laboratories.
2. Identify capacities and opportunities for maintaining regional achievements and meeting the challenges of a Network of VPD Laboratories.
3. Consider strategies for strengthening the response capacities and the performance of labs of the Regional Network of VPD Laboratories, information flows, communications, compliance with indicators and monitoring of national laboratory networks.

Technical presentations and discussions addressed the following topics:

- Status of VPDs in the Region;
- Essential role of the VPD Lab Network, its achievements and challenges;
- Experiences of sentinel hospital surveillance of pneumonias and diarrheas caused by rotavirus
- Achievements and challenges of the Invasive Bacterial Disease Lab Network;
- Experiences of the integration and quality control of Mexico's national measles/rubella laboratory network;
- Experiences of the implementation of a national lab network to support HPV surveillance in Argentina; and
- Past and future of lab diagnostics of pertussis.



**The main conclusions and recommendations were the following:**

The Laboratory Network of the Americas has been providing support for VPD eradication, elimination, and control initiatives as soon as they have been approved by the PAHO's Governing Bodies. Polio and measles/rubella Lab Networks have provided support to surveillance of these diseases and contributed important and relevant information for decision-making and the steering of national immunization programs.

The essential role of the laboratory is to provide accurate, reliable and timely information that helps guide resource use for the control, elimination and eradication of diseases, as well as to support the documentation of the impact of the introductions of new vaccines.

Surveillance and labs are essential components of an effective immunizations program and are needed for strategic and evidence based decision-making.

Country representatives reaffirmed the need to promote the integration of data generated by laboratories with that of epidemiological surveillance, in order to enable the comprehensive analysis of VPDs at the national and regional levels. Along these lines, they expressed the need to review the regulatory frameworks in countries to promote that immunization, lab and surveillance be integrated with the epidemiological surveillance system.

It is important to guarantee the compliance with the indicators that have been defined for VPD surveillance. To this end, the lab performance indicators should be included in surveillance information systems and reported to the Ministries of Health and to PAHO/WHO.

In order to facilitate the comparability of lab results between countries, it is recommended that labs in the Network harmonize the different procedures they use to identify serotypes/ serogroups/ genotypes of the pathogens that cause VPDs. It was also suggested that a website should host the different test protocols used by the Regional Laboratory Network.

Lab diagnostics of pertussis are done through culture, PCR, serology and immunofluorescence, this last one is not recommended as it has low sensitivity and specificity. Test selection should consider the stage of the disease, the quality of the specimen, previous antibiotic treatments and test standardization. Tests are complimentary and more than one can be used simultaneously.

Cultures can be positive during the first two weeks of symptoms, PCR can be positive up to four weeks after the onset of symptoms, and serology can often be positive after two weeks and maximum 12 weeks after the onset of symptoms.

PCR has the highest sensibility but can present false positives when it is only amplified to the IS481 region. In order to improve PCR's specificity, it is recommended to use the PCR multiplex (CDC), which amplifies 4 regions of the bacteria's genome: ptxS1, IS481, hIS1001, pIS1001 allowing the identification of the three *Bordetella* species and identify mixed infections.



In order to support impact evaluations of HPV vaccination, a highly sensitive test is required to be able to identify and typify the HPV genotypes present in the specimen. Molecular biology tests should, at minimum, have the capacity to detect and typify high risk genotypes 16, 18 and low risk 6 and 11.

In house tests that combine PCR with reverse hybridization that have been validated by WHO HPV LabNet have demonstrated a good level of performance. Currently there are several commercial tests with similar techniques, validated by the manufacturers, that have adequate reproducibility and sensitivity, however, their cost is still high for Latin American and Caribbean countries. It is recommended that labs carry out these tests and participate in an external quality assessment program.

The accreditation of national labs should be continued in accordance to the criteria defined by the WHO/PAHO and the official accreditation should be communicated to national authorities.

National laboratories should promote the integration of public and private laboratories running diagnostic tests on VPDs into national networks. They should consider meetings and training activities that would foster strategic alliances.

National labs should comply with the roles outlined in PAHO's Guide for Sentinel Hospital Surveillance, specifically those related to quality control of sentinel labs, diagnostic confirmation and typification. It is essential that labs participating in SIREVA II be integrated into the countries' surveillance systems.

Given that labs are an essential component of surveillance systems, adequate resource allocation to enable compliance with their essential role within those systems should be considered in national budgets, in order to guarantee the sustainability of the labs' functions.

With the aim of facilitating the VPD labs' access to reagents for surveillance, it was requested that the PAHO's Revolving Fund for vaccine purchase find alternatives to enable the procurement of these products.

It was also requested that PAHO continue providing technical cooperation to strengthen the response capabilities of the Regional Laboratory Network and to maintain the Network support to expert groups and strategic partners.

The need to consider the feasibility and relevance of establishing a Network of VPD Laboratories arises in response to the advent of new vaccine introductions that require the addition of new labs and new diagnostic methods. This Network would ideally guarantee the lab services necessary for the surveillance of these events; it would optimize the existing lab capacities; facilitate communications within and outside the institution and promote a greater resource mobilization.



At the meeting closing, PAHO recognized the efforts of national laboratories in supporting the VPD surveillance, their essential role in identifying the serotypes/serogroups/genotypes, information needed for disease burden studies and for measuring the impact of the introduction of new vaccines.

