

**Technical Advisory Group on Vaccine-preventable Diseases (TAG)  
XXII Meeting  
Washington DC, 1-2 July, 2014**



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## Table of Contents

<b>TAG MEMBERS .....</b>	<b>3</b>
<b>ACRONYMS.....</b>	<b>5</b>
<b>INTRODUCTION .....</b>	<b>7</b>
<b>UPDATE ON THE REGIONAL IMMUNIZATION PROGRAM OF THE AMERICAS .....</b>	<b>9</b>
<b>UPDATE ON IMPLEMENTATION OF TAG RECOMMENDATIONS ON THE POLIO ERADICATION AND ENDGAME STRATEGIC PLAN 2013-2018 .....</b>	<b>11</b>
RECOMMENDATIONS .....	13
<b>STATUS OF HUMAN PAPILLOMA VIRUS VACCINATION .....</b>	<b>16</b>
RECOMMENDATIONS: .....	17
<b>STATUS OF INFLUENZA VACCINATION IN THE AMERICAS AND FORMATION OF THE NETWORK FOR EVALUATION OF INFLUENZA VACCINE EFFECTIVENESS—REVELAC-I .....</b>	<b>18</b>
RECOMMENDATIONS: .....	19
<b>CHOLERA VACCINATION IN THE AMERICAS .....</b>	<b>21</b>
RECOMMENDATIONS: .....	22
<b>STATUS OF THE DOCUMENTATION AND VERIFICATION PROCESS OF THE ELIMINATION OF MEASLES, RUBELLA, AND CONGENITAL RUBELLA SYNDROME .....</b>	<b>23</b>
RECOMMENDATIONS: .....	25
<b>UPDATE ON PERTUSSIS VACCINATION .....</b>	<b>26</b>
RECOMMENDATIONS: .....	27
<b>UPDATE ON THE PAHO REVOLVING FUND .....</b>	<b>29</b>
RECOMMENDATIONS: .....	30
<b>UPDATE ON IMMUNIZATION DATA QUALITY AND ELECTRONIC IMMUNIZATION REGISTRIES .....</b>	<b>31</b>
RECOMMENDATIONS .....	34
<b>VACCINATION WITH PNEUMOCOCCAL CONJUGATE VACCINE IN ADULTS.....</b>	<b>35</b>
RECOMMENDATIONS: .....	36
<b>TOOLS FOR IMPROVING THE EFFECTIVE MANAGEMENT OF IMMUNIZATION PROGRAMS AT ALL LEVELS .....</b>	<b>38</b>
RECOMMENDATIONS: .....	39

## TAG Members

**Dr. Peter Figueroa**

Professor Public Health  
Epidemiology & HIV/AIDS  
University of the West Indies  
Kingston, Jamaica

**Chair *a.i***

**Dr. Akira Homma**

Chairman of Policy and Strategy Council  
Bio-Manguinhos Institute  
Rio de Janeiro, Brazil

**Dr. Anne Schuchat**

Director  
National Center for Immunization and Respiratory Diseases  
Centers for Disease Control and Prevention  
Atlanta, GA, United States

**Dr. Anushua Sinha**

Associate Professor  
UMDNJ New Jersey Medical School  
Newark, NJ, United States

**Dr. Arlene King**

Professor  
Dalla Lana Faculty of Public Health  
University of Toronto  
Toronto, Ontario, Canada

**Dr. Jeanette Vega\***

Director  
Chile's National Health Fund  
Santiago, Chile

**Dr. José Ignacio Santos**

Professor  
Experimental Medicine Unit  
Faculty of Medicine of the National Autonomous University of  
Mexico  
Mexico City, Mexico

**Roger Glass\***

Director

Fogarty International Center & Associate Director for  
International Research, NIH/JEFIC-National Institutes of Health  
Bethesda, M.D., United States

**Dr. Cuauhtémoc Ruiz Matus**

Unit Chief, Comprehensive Family Immunization

PAHO/WHO

Washington, D.C., United States

*Ad hoc Secretary*

**\* Not present at TAG 2014**

## Acronyms

aP	Acellular Pertussis
AFP	Acute Flaccid Paralysis
CDC	Centers for Disease Control and Prevention of the United States
CRS	Congenital Rubella Syndrome
cVDPV	(Circulating) Vaccine-derived Poliovirus
DHS	Demographic and Health Surveys
DPT3	Third dose of the Diphtheria-Pertussis-Tetanus vaccine
DQS	Data Quality Self-assessment
DoV	Decade of Vaccines
EIR	Electronic Immunization Registry
EMRO	Eastern Mediterranean Region of the World Health Organization
EPI	Expanded Program on Immunization
GACVS	Global Advisory Committee on Vaccine Safety
GNI	Gross National Income
GVAP	Global Vaccine Action Plan
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
IBD	Invasive Bacterial Disease
ICG	International Coordination Group
IDQi	Project for Improving Data Quality for Immunization
IHR	International Health Regulations
IPD	Invasive Pneumococcal Disease
IEC	International Expert Committee (for the documentation and verification of measles, rubella, and congenital rubella syndrome elimination in the Americas)
IPV	Inactivated Polio Vaccine
JRF	PAHO-WHO/UNICEF Joint Reporting Form on Immunization
LAC	Latin America and the Caribbean
MICS	Multiple Indicator Cluster Survey
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
M&E	Monitoring and Evaluation
NIP	National Immunization Program
NNT	Neonatal tetanus
OCV	Oral Cholera Vaccine
OPV	Oral Polio Vaccine

bOPV	Bivalent Oral Polio Vaccine
mOPV	Monovalent Oral Polio Vaccine
tOPV	Trivalent Oral Polio Vaccine
PAHO	Pan American Health Organization
PEES	Polio Eradication and Endgame Strategic plan
PHEIC	Public Health Emergency of International Concern
Spn	<i>Streptococcus pneumoniae</i>
PCV	Pneumococcal Conjugate Vaccine
PCV13	Pneumococcal Conjugate Vaccine 13-Valent
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 World Health Organization)
SARI	Severe Acute Respiratory Infection
TAG	Technical Advisory Group on Vaccine-preventable Diseases
Tdap	Tetanus Toxoid Acellular Pertussis Vaccine (for adolescents and adults)
TEPHINET	Training Programs in Epidemiology and Public Health Interventions Network
UNICEF	United Nations Children's Fund
VE	Vaccine Effectiveness
VWA	Vaccination Week in the Americas
WASH	A nonprofit, nonpartisan initiative dedicated to helping solve the global safe drinking Water, Sanitation, and Hygiene challenge
WHA	World Health Assembly
WHO	World Health Organization
wP	Whole-cell Pertussis
WPV	Wild Poliovirus
WPV1	Wild Poliovirus type 1
WPV2	Wild Poliovirus type 2
WUENIC	WHO/UNICEF Estimates of National Immunization Coverage

## Introduction

The XXII Meeting the Technical Advisory Group (TAG) on Vaccine-preventable Diseases of the Pan American Health Organization (PAHO) was held in Washington, DC, United States on 1-2 July 2014. The slogan for the meeting was “Vaccination: your best shot!”, chosen in the context of the FIFA Football (Soccer) World Cup taking place at the same time in Brazil. This meeting’s objective was to review progress on selected topics and issue recommendations to address pressing challenges faced by national immunizations programs in the Americas.

PAHO’s Assistant Director, Dr. Francisco Becerra, welcomed the participants and gave a brief introduction to the TAG’s charge as regional technical advisory group on vaccine-preventable diseases. This TAG meeting was marked by the recent passing of Dr. Ciro de Quadros, TAG President since 2004. Before starting the meeting, Dr. Peter Figueroa asked the audience for a minute of silence in memory of Dr. de Quadros. Dr. Jon Andrus, PAHO Deputy Director, shared reflections to honor Dr. Ciro de Quadros. Dr. de Quadros led the Immunization Program of the Americas at PAHO between 1977 and 2002, after having worked in a rural area of the Amazon in his native Brazil and for the World Health Organization in smallpox eradication in Ethiopia. During his tenure at PAHO, Dr. de Quadros oversaw the implementation of the regional Expanded Program on Immunization (EPI) and led the polio and measles elimination efforts. More recently, he actively contributed to global level policy development and promoted evidence-based decision-making worldwide in his role as Executive Vice-President of the Sabin Vaccine Institute. He was also instrumental in the development and endorsement of the Global Vaccine Action Plan (GVAP), the framework of the Decade of Vaccines (DoV) initiative that seeks to expand the benefits of vaccination to everybody regardless of where a person was born or lives.

Dr. de Quadros was a public health visionary and strategist, and he viewed vaccination as a human right. Through vision, diplomacy and persistence he not only helped the Region of the Americas pioneer disease elimination, but also forged partnerships that led to making the EPI of the Americas the most successful immunization program in the world. In 1995, he created PAHO’s TAG as an advisory body for polio elimination, and later expanded its mandate to provide guidance on vaccine-preventable diseases and the full immunization program. Dr. de Quadros received many awards during his life. One of the closest to his heart was the “Public Health Hero of the Americas” award presented to him by PAHO’s Director Dr. Carissa F. Etienne, in April 2014, roughly a month before his death.

Dr. de Quadros donated the money he received as part of the Prince Mahidol Award, an annual award given by the Thai Royal Family for outstanding achievements in medicine and public health worldwide, to create the Regional Immunization Award. This Award has been proposed to be renamed the “Ciro de Quadros Immunization Award”.

Dr. Peter Figueroa chaired the meeting *ad interim*. TAG members acknowledged the contributions of PAHO's Secretariat to the success of the meeting and issued this report in memory of Dr. Ciro de Quadros.

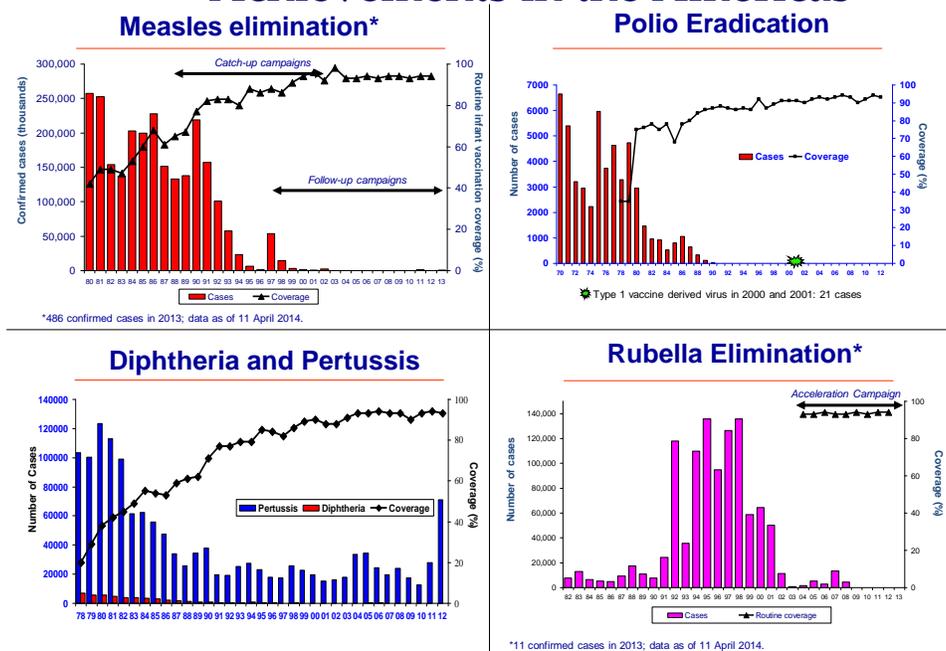
## Update on the Regional Immunization Program of the Americas

The most recently available data on the situation of vaccine-preventable diseases (VPDs) and the immunization program of the Americas were presented, under the framework of the Regional Immunization Vision and Strategy (RIVS). The Region is working to present the regional adaptation of the Global Vaccine Action Plan (GVAP) to PAHO's Directing Council in 2015. Data for topics discussed during the XXII meeting of the Technical Advisory Group (TAG) were not presented in detail in this overview.

### Maintaining the Achievements

Coverage levels have remained over 90% throughout the Region and work is ongoing to maintain VPD control and elimination.

## Achievements in the Americas



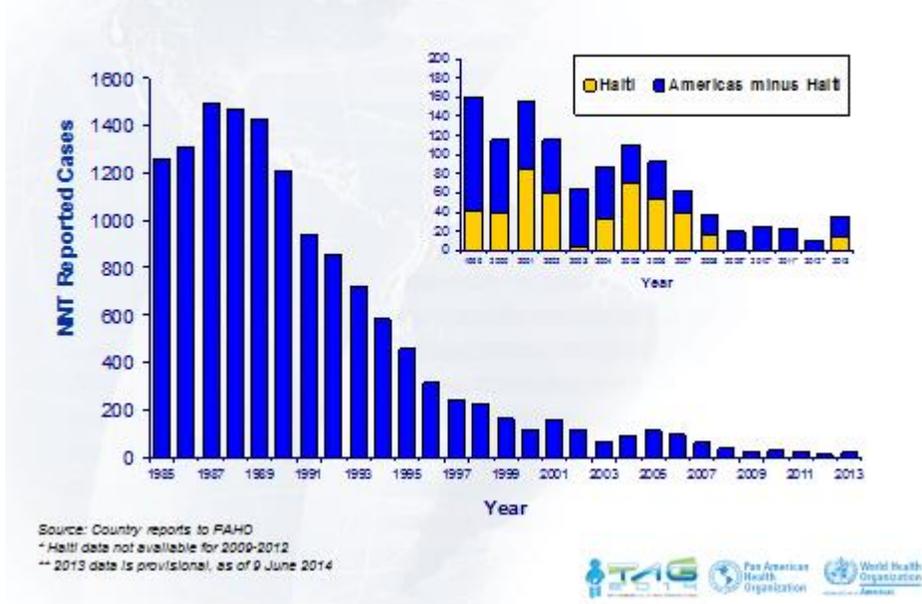
Available preliminary data for 2013, however, suggests that regional DTP3 and Polio3 coverage may have declined compared to previous years. This situation is being examined.

### Addressing the Unfinished Immunization Agenda

Work in this area has revolved around targeting underperforming municipalities and areas within countries. Latin American countries have identified risk areas based on coverage, VPD surveillance performance, and other socio-demographic and contextual factors. It is of concern that half of the ~15,000 municipalities in Latin America and the Caribbean (LAC) don't reach coverage rates  $\geq 95\%$ . Furthermore, it is also concerning that there are several municipalities, concentrated in a few countries, reporting coverage levels  $< 50\%$ .

Since its creation in 2003, Vaccination Week in the Americas (VWA) has served as a platform to target vulnerable populations every year. In 2014, VWA’s slogan was “Vaccination: Your best shot!” in acknowledgment of the FIFA World Cup of Football (Soccer) taking place in Brazil. Finally, an important part of the unfinished agenda is the elimination of neonatal tetanus (NNT) as a public health problem<sup>1</sup> in Haiti. While cases have continued to decline over the years, elimination has proven challenging.

### Neonatal Tetanus Elimination, The Americas 1985-2013



#### Meeting New Challenges

The introduction of new more expensive vaccines has been one of the main challenges immunization programs of the Americas have faced in recent years. About 90% of the birth cohort in the Region lives in countries that have introduced a pneumococcal conjugate vaccine in their regular program (~60% of the cohort of LAC); ~87% of cohort is living in countries that have introduced rotavirus vaccine (60% of the cohort of LAC), and ~75% of girls 10-14 years old live in countries that have introduced a human papilloma virus (HPV) vaccine.

#### Operational Activities

Of all the EPI components that the RIVS identifies as components requiring additional strengthening, cold chain and supply chain operations, syringe quality control program, economic evaluations (i.e. the ProVac Initiative), and vaccine effectiveness studies for rotavirus and conjugated pneumococcal vaccines were highlighted during this meeting. Finally, the Revolving Fund for Vaccine Procurement was mentioned in the context of sustainability, as LAC countries finance >90% of national EPIs with national funds.

<sup>1</sup> NNT elimination is defined as <1 case of NNT per 1,000 live births in every municipality.

## Update on Implementation of TAG Recommendations on the Polio Eradication and Endgame Strategic Plan 2013-2018

### **Background**

The Polio Eradication and Endgame Strategic plan (PEES), as approved by the Executive Committee of the WHO in January 2013, has 4 main objectives:

1. Detection and interruption of poliovirus transmission.
2. Strengthening of systematic immunization programs and withdrawal of the oral polio vaccine.
3. Containment and certification.
4. Delivery plan for the legacy of polio eradication.

The principal activities proposed by WHO for implementation of the Polio Eradication and Endgame Strategic Plan, 2013-2018 are:

- Strengthen epidemiological surveillance to rapidly detect any poliovirus importation. Acute flaccid paralysis (AFP) surveillance remains the primary mechanism for the detection of poliovirus. In addition, environmental surveillance can complement AFP surveillance for detecting the presence of poliovirus in selected areas and populations.
- Increase vaccination coverage. Reach and maintain vaccination coverage  $\geq 95\%$  in all districts and municipalities.
- Introduce at least one dose of the inactivated polio vaccine (IPV) in vaccination schedules for every country. The strategic plan establishes that the type 2 vaccine virus must be removed from the oral vaccine by mid-2016. Before its removal, all countries must introduce at least one additional dose of IPV by the end of 2015.
- Certify eradication and containment of all polioviruses by the end of 2018. Safe management and containment of infectious and potentially infectious materials in laboratories will be essential to minimize the risk of wild poliovirus reintroduction following interruption of global transmission.
- Contribute to reaching other health goals through the transfer of acquired knowledge and experiences gained through the polio eradication process.

In April 2014, an extraordinary meeting of the TAG was convened to review and discuss the adoption of this plan in the Americas. This report has been widely circulated in the Region.

### ***Current status of implementation of the Polio Eradication and Endgame Strategic Plan in the Americas***

The countries of the Region have given continuity to epidemiological surveillance of AFP cases in children under 15 years of age. Since 1986, the Region has met the target set for the AFP reporting rate indicator; however, the rate is not uniform among all countries. For example, the percentage of cases with adequate samples has ranged between 79% and 73% over the last 10 years, with the fewest number of adequate samples in 2013. Also, the percentage of cases investigated in the first 48 hours has not exceeded 80% in the last 2 years, reaching only 75% and 61% in 2012 and 2013, respectively.

Currently, routine environmental surveillance has been conducted only in the state of São Paulo in Brazil. Through this surveillance the country was able to detect an imported wild poliovirus in a sample collected in the residual waters of the Viracopos airport in March 2014. This type of complimentary surveillance is being evaluated for use in other select countries.

The countries of the Region continue working to reach and to maintain adequate vaccination coverage through different strategies, implemented both in the regular program and in supplementary vaccination campaigns. Countries are also taking advantage of the opportunity of Vaccination Week of the Americas to intensify vaccination in remote areas and vulnerable communities. Furthermore, the endorsed collaboration between Canada and PAHO has helped countries strengthen various components of the EPI in priority areas and municipalities, seeking to increase vaccination coverage.

The Region has made substantial progress in the introduction of at least one dose of IPV. To date, 14 countries in the Region are using IPV in their routine vaccination schedules during the first year of life, which corresponds to 65% coverage of the birth cohort in the Region. PAHO will continue to support countries in decision-making and in the process of introducing at least one dose of this vaccine to their basic vaccination schedules against polio.

The Regional Certification Commission is in the process of formalizing its formation and the first meeting of the commission should be held this year. In 2010, the Region completed the first phase in the process of containment of infectious or potentially infectious materials. WHO is reviewing the guidelines for the second phase of containment and should issue its recommendations in the coming months. The countries of the Americas have not created any special structure to achieve the polio eradication objective, but have instead strengthened the regular EPI. In 1995, PAHO formed a Commission to evaluate how the eradication process had affected country health systems. The final report "Taylor Commission," titled as such because it was chaired by Dr. Carl Taylor, emeritus professor at the School of Public Health at Johns Hopkins University in the United States, documents the lessons learned and the positive impact of the polio eradication program on health services in the Region.

On 5 May 2014, the Director-General of WHO declared the international spread of wild poliovirus in 2014 a Public Health Emergency of International Concern (PHEIC). The current situation of the international spread of wild polioviruses in 2014 to date is in contrast to the near-cessation of international spread of wild poliovirus from January 2012 through 2013, low transmission season for this disease (i.e. January to April). If not properly responded to, this situation could put the global eradication goal at risk.

The Director-General endorsed the following recommendations provided by the International Health Regulations Emergency Committee that was convened on 28-29 April 2014:

- All states that are currently exporting wild poliovirus (Pakistan, Cameroon, and the Syrian Arab Republic) pose the greatest risk of further exportations and should ensure that all residents and long-term visitors receive a dose of OPV or IPV between 4 weeks and 12 months prior to international travel.
- States Infected with Wild Poliovirus but Not Currently Exporting (Afghanistan, Equatorial Guinea\*, Ethiopia, Iraq, Israel, Somalia and particularly Nigeria) also pose a risk to exportation and should encourage residents and long-term visitors to also receive a dose of OPV or IPV 4 weeks to 12 months prior to travel.

\*At the time these recommendations were made, there were no reported exportations from Equatorial Guinea. Since then, on 18 June, an isolate of WPV1 was detected in Brazil that indicated a close match with a strain of WPV1 that was recently isolated from a case of polio in Equatorial Guinea. According to the International Health Regulations (IHR) temporary recommendations issued by the Director-General of WHO on 5 May 2014, Equatorial Guinea is considered a polio exporting country. The country should therefore ensure that all residents and long-term visitors (of more than 4 weeks) who travel internationally receive a supplementary dose of the polio vaccine between 4 weeks and 12 months prior to departure.

#### **Recommendations:**

- TAG expresses concern regarding the reported decline in Polio3 coverage at the national and sub-national levels in the Americas. As such, TAG strongly urges countries to ensure high, homogenous polio coverage to maintain the achievement of polio elimination in the Region.
- TAG notes the confirmed isolation of WPV1 in Brazil from environmental sampling in the state of Sao Paulo in March 2014 and commends Brazil for its response to this isolation. This finding confirms that the risk of WPV is real for the Region.
- In light of the newly confirmed risk of WPV importation in the Americas, TAG calls upon PAHO Member States to urgently take action to strengthen AFP active surveillance. The

reported decline in the proportion of laboratory specimens of quality collected and timeliness of case investigations jeopardizes the opportune detection of imported WPV (or VDPVs) and rapid deployment of response activities.

- Due to its high cost and involved methods, expansion of environmental surveillance networks in the Region needs further assessment. TAG recommends that PAHO assess the strengths and weaknesses of existing environmental sampling methods and based on this risk assessment and evaluation of existing methods, PAHO should propose potential options for environmental sampling in selected settings in the Region.
- PAHO should conduct a risk analysis to identify areas in the Region with a high concentration of WPV importation (and VDPV) risk (i.e. geographic areas with suboptimal polio3 coverage and a large number of international visitors from polio endemic or at risk areas).
- TAG reiterates the recommendations issued during the extraordinary TAG Meeting on Polio conducted in April 2014:
  - TAG agrees with the renewed efforts towards eradicating polio and the objectives of the polio endgame. These efforts include the ongoing removal of Sabin oral polio vaccine from the routine immunization schedule.
  - TAG reiterates its previous recommendations, emphasizing:
    - The importance of achieving and maintaining high and homogenous vaccination coverage rates to reduce risk of importations of WPV and cVDPV, and
    - The need for continued strengthening of epidemiological AFP surveillance.
  - TAG urges implementation of environmental surveillance towards validating the elimination of cVDPVs and WPV.
  - TAG agrees with the six prerequisites stated by SAGE to switch from tOPV to bOPV.\*
  - The countries of the Americas are already in the process of introducing IPV. At the end of 2015, approximately 80% of the birth cohort in the Americas will be covered with IPV. PAHO is providing technical cooperation to the countries on this process.
  - The remaining countries must decide when they will be able to introduce IPV, taking into consideration affordability (price for vaccines and operational costs), current opportunity costs, and sustainability. PAHO should continue working with the countries to help remove barriers for such introduction.
  - When introducing IPV, countries should consider sequential schedules. Ideally, countries should consider two IPV doses followed by two OPV doses. However, if a country is considering only one IPV dose, this should be with the first DTP dose and followed by three OPV doses.
  - Countries should not consider moving directly to an IPV only schedule at this time, unless they meet the criteria previously recommended by TAG and WHO

(low risk of transmission and importation, high homogeneous coverage, and good sanitation).

\*According to the SAGE's recommendations, prior to the withdrawal of OPV2 – by replacing tOPV with bOPV in all OPV-using countries, six prerequisites must be in place:

1. Validation of the elimination of persistent cVDPV type 2 and confirmation of WPV2 eradication;
2. A mOPV type 2 stockpile and response capacity;
3. Surveillance capacity and an international notification requirement for all Sabin, Sabin-like, and cVDPV type 2 viruses;
4. Sufficient bOPV products for all OPV-using countries;
5. Affordable IPV option(s) for all OPV-using countries;
6. Phase II bio-containment of all cVDPVs type 2 and WPV.

## Status of Human Papilloma Virus Vaccination

As of June 2014, 21 countries and territories in the Americas have introduced the vaccine against human papillomavirus (HPV) in their publicly funded immunization programs. Notably, Brazil introduced the HPV vaccine in March 2014 and 4.2 million Brazilian girls aged 11–13 years (85.3% of the target population) received the first vaccine dose by the end of June. Compared to the Sub regions of North America, the Southern Cone and the Andes, fewer countries in Central America and the Caribbean have introduced the HPV vaccine. Overall, an estimated 83% of a typical birth cohort of adolescent girls (6.3 million girls) has in principle access to HPV immunization in the Americas.

However, data on HPV vaccination coverage are limited. Only one country publishes coverage data each year, which are estimated through nation-wide surveys. For 2012—the sixth year of vaccination in this country – the estimated first-dose coverage in girls aged 13 years was 47%; drop-out between the first dose and the dose given after six months was 57%. For the same year, nine countries reported the number of administered HPV vaccine doses in their UNICEF/WHO Joint Reporting Forms (JRF); overall, 8.7 million doses were administered. For the four countries with adequate data for analysis (4.7 million doses administered), first-dose coverage ranged from 51% to 81%. Drop-out between the first dose and the dose given after six months ranged from 14% to 41% for the three countries with a classical 3-dose immunization schedule and was 48% for the country with an extended 3-dose immunization schedule. Although limited, these coverage data indicate that real access to and/or acceptability of the HPV vaccine and the monitoring of vaccinated cohorts remain deficient.

In July 2013, TAG recommended extended HPV immunization schedules for adolescents aged <14 years. TAG considered that these schedules could offer immunological, programmatic and financial advantages. In April 2014, WHO's Strategic Advisory Group of Experts on Immunization (SAGE) discussed the same issue. Specifically, SAGE considered that vaccine-induced antibodies mediate HPV vaccine efficacy and that, as immunobridging studies show, adolescent women had similar or higher antibody titers than adult women. SAGE also considered a systematic review of randomized and non-randomized studies and a descriptive review of observational studies, as well as the findings of an ad-hoc expert consultation on HPV immunization schedules. SAGE concluded that, based on immunologic evidence, a 2-dose extended schedule with a minimum interval of six months administered to adolescent women was non-inferior to a 3-dose classical schedule administered to adolescent and adult women. SAGE recognized that the potential of reducing the dose schedule from 3 to 2 and the flexibility in intervals between doses may lead to improvement in vaccination coverage.

Despite concerns by the public and some health professionals, the HPV vaccine is safe. In 2013–2014, WHO's Global Advisory Committee on Vaccine Safety (GACVS) reviewed the occurrence of events supposedly attributed to HPV vaccine and immunization at three occasions, namely in June and December 2013, and March 2014. At the last occasion, GACVS stated that “it is

important to highlight and reiterate [these reviews] because a number of national immunization programs have been facing real and potential public losses of confidence in their programs as a result of increased negative publicity, even from safety issues that have been addressed.” The efforts made by immunization programs to guarantee safe vaccine development and administration, the characteristics of today’s HPV vaccines, the data generated in the controlled clinical trials, and the data emerging from post-marketing active surveillance and large and lengthy studies are the four elements that underpin HPV vaccine safety.

Emerging evidence shows the effectiveness of HPV immunization programs in reducing HPV infections and precancerous cervical lesions among young women. HPV immunization has a real potential to curb the burden of HPV-related cancers within a generation. However, the realization of this potential depends on a greater uptake and acceptability of the HPV vaccine by the public and health professionals alike.

### **Recommendations:**

- TAG affirms the sound and robust evidence base that demonstrates the safety and efficacy of HPV vaccines among adolescent and young women. TAG also endorses the March 2014 and prior GACVS statements related to HPV vaccine safety. As such, TAG continues to encourage countries to adopt HPV vaccines in the routine national immunization schedule to prevent cervical cancer. To harmonize regional and global recommendations on HPV immunization schedules, TAG endorses the April 2014 SAGE recommendations. Specifically,
  - A 2-dose schedule with an interval of at least six months between doses is recommended for girls aged <15 years of age. This also applies to girls aged ≥15 years at the time of the second dose. If for any reason the interval between the first and second dose is shorter than 5 full months, a third dose should then be given ≥6 months after the first dose.
  - The 3-dose schedule (0, 1/2, 6 months) remains recommended for girls aged >15 years (when immunization is initiated) and for immunocompromised individuals of all ages, including those known to be HIV-positive;
  - These schedule recommendations apply to both the bivalent and tetravalent vaccines.
- Manufacturers and countries should work towards the harmonization of licensure information with recommended schedules at national level.
- TAG reaffirms that it is important for countries that are considering the introduction of the HPV vaccine, to carefully plan information systems to collect and analyze coverage data at all levels. Countries that have already introduced an HPV vaccine should strengthen their efforts to characterize vaccination coverage at subnational and national levels.
- TAG expresses concerns about the estimated low HPV vaccine coverage and high drop-out rate, which may indicate significant barriers, from parents and/or health workers, to access or lack of follow-up. TAG recommends that countries gather data to characterize these issues and to develop communication strategies to address them.

## Status of Influenza Vaccination in the Americas and Formation of the Network for Evaluation of Influenza Vaccine Effectiveness—REVELAC-i

The Region of the Americas has made considerable strides in the introduction of the seasonal influenza vaccine. By 2013, 40 of the 45 countries and territories of the Americas were using the seasonal influenza vaccine in the public sector to protect one or more risk groups. This includes 40 countries and territories that vaccinate the elderly, 39 that vaccinate health workers, 30 that vaccinate children (5 of them only children with chronic diseases), and 36 that vaccinate adults with chronic diseases. Great progress has been made in the vaccination of pregnant women, growing from 7 countries in 2008 to 26 countries in 2013.

To guide vaccine policy, especially during the last decade, countries located in tropical areas, especially in Central America, have worked to improve surveillance systems for the influenza virus in the sub-region. However, there are still uncertainties about the most appropriate timing and formulation for vaccination in this sub-region. A similar situation is observed in countries such as Peru with two influenza circulation patterns during the year.

In this context of successes and challenges in the Region, it is important to know the performance of this vaccine, yet there have been few effectiveness studies of the influenza vaccine in Latin America and the Caribbean (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.

In this context, during 2012, a pilot was carried out in four Central American countries to evaluate the effectiveness of the influenza vaccine, using the existing severe acute respiratory infection (SARI) surveillance platforms already in these countries. This was a collaborative project among the United States Centers for Disease Control and Prevention (CDC), Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), and PAHO. The project took advantage of the lessons learned from the pilot and the official creation of the Network for Evaluation of Influenza Vaccine Effectiveness in Latin America and the Caribbean (REVELAC-i) in February 2013. That same year, the project was implemented in Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Honduras, Panama, and Paraguay during the 2013 influenza season.

The objective was to estimate effectiveness of the trivalent seasonal influenza vaccine in preventing SARI from influenza in the target vaccination groups (children and the elderly) that go to sentinel hospitals for SARI, using a test-negative case-control design. The nine countries participated with 71 sentinel hospitals.

The information on vaccination was completed using electronic immunization registries or paper records from the EPI, vaccination certificates, clinical files, and occasionally through

home visits. A patient was considered vaccinated if he or she had received at least one dose of vaccine more than two weeks before symptom onset.

As of 18 March 2014, 8 countries had reported a total of 2,395 SARI cases (627 influenza cases and 1,768 controls). The analysis included 1,865 patients: 144 influenza cases and 454 controls in children and 342 cases and 925 controls in the elderly. The greatest concentration of influenza cases was found in June and July [mainly influenza A (H1N1) pdm09 followed by A (H3N2) and influenza B], and circulation of the virus was recorded until December.

Crude vaccine effectiveness (VE) in children was 48% [22% to 66%], and 52% [36% to 72%] adjusted by week of symptom onset. In the elderly, crude VE was 57% [43% to 68%], 59% [45% to 79%] adjusted by week of symptom onset, and 57% [41% to 68%] adjusted by age group (60-69 years; 70-79 years, and ≥80 years). VE for influenza A (H1N1) pdm09 was 57% [14% to 79%] in children and 70% [53% to 80%] in the elderly. The moderate VE estimated in Latin America coincides with reported estimates from hospital-based studies in the Southern Hemisphere (Australia and New Zealand) and vaccination continues to be the best available prevention measure against complications and deaths due to influenza.

The REVELAC-i platform offers the opportunity to:

- Systematically evaluate VE using the existing sentinel hospital platform in countries.
- Continue integration of epidemiological surveillance, laboratory, and immunization programs to produce evidence for decision-making on influenza virus prevention and control.
- Explore the integration of sentinel surveillance for viral respiratory diseases with bacterial respiratory diseases using the REVELAC-i platform.
- Develop mechanisms to share experiences, lessons learned, and common methods among countries and research centers on influenza vaccine effectiveness, as well as for learning the impact of influenza vaccination.
- Conduct other evaluations, such as the effect of influenza vaccination on newborns in cohorts of pregnant women.
- Conduct knowledge, attitudes, and practices surveys on influenza vaccination, among others.

#### **Recommendations:**

- TAG notes the progress made in influenza vaccine use and urges countries to expand the use of this vaccine and achieve higher coverage rates, in line with previous TAG and SAGE recommendations with an emphasis on pregnant women and health care workers.
- The TAG applauds the formation and progress of the Network for Evaluation of Influenza Vaccine Effectiveness (REVELAC-i) and encourages Latin American and Caribbean countries to continue to produce evidence on the performance and impact of the influenza vaccine; and to strengthen the integration among immunization, epidemiology, and laboratory.

- PAHO should support the continued strengthening of influenza surveillance and should analyze and present the data by geographical areas within countries, particularly in larger countries where the influenza epidemiology and seasonality varies by region.
- PAHO should continue to provide guidance to countries on choosing the most adequate vaccine for their epidemiological and contextual situation.

## Cholera Vaccination in the Americas

In 2013, cholera transmission was reported in four countries of the Americas—Cuba, Haiti, Mexico, and the Dominican Republic. Although transmission in Haiti has declined significantly since cholera emerged in October 2010, the country is still reporting the greatest incidence in the Region. During the 12 months from June 2013 to May 2014, 44,867 cholera cases and 450 cholera-related deaths were recorded in Haiti. In contrast, during the 12 months from October 2010 to September 2011, 464,670 cases and 6,555 deaths were reported—10 and 15 times greater, respectively, than in the most-recent 12-month period.

Deployment of oral cholera vaccine (OCV) has been considered since October 2010. At that time, PAHO recommended focusing emergency efforts on time-tested measures for cholera outbreak response. An expert consultation convened by PAHO in December 2010 recommended that the limited vaccine supply be used for demonstration projects and that efforts be taken to increase OCV availability. Between April and June 2012 two non-governmental organizations, GHESKIO and Zanmi Lasante/Partners in Health, conducted separate but coordinated cholera vaccination of nearly 100,000 people in one urban and one rural area of Haiti. In July–August 2013, the Haitian Ministry of Health vaccinated an additional 120,000 people in two localities.

TAG discussed the use of the oral cholera vaccine (OCV) in October 2012 with a focus on the Island of Hispaniola. As part of a regional initiative for elimination of cholera transmission on the Island, TAG recommended deployment of OCV in Haiti to mitigate the cholera burden in the short and medium term, until significant and sustainable advances are achieved in infrastructure for drinking water supply and sanitation. TAG's recommendations were adopted in the "National Plan for the Elimination of Cholera in Haiti, 2013–2020," which the Haitian Government issued in February 2013.

In Haiti, approximately 200,000 people received at least one dose of OCV in 2012–2013. These experiences demonstrate the feasibility of vaccination against cholera; second-dose coverage, measured with surveys, ranged from 63% to 77%. There are plans to vaccinate an additional 200,000 people in July and August 2014. The results of a clinical trial in an endemic area of Calcutta, India, show that OCV can have an effectiveness of 65% in the five years after vaccination.

The occurrence of cholera in Cuba and Mexico not only underscores the risk of importations, but also that indigenous transmission can occur after an importation. Although the cholera epidemic of the 1990s, which affected 21 countries of the Region, finally caused improvements in access to drinking water and sanitation, conditions that enable cholera transmission persist to different extents in some areas of all of the countries of the Region. For example, in 2010 in Central America, an estimated 12.7 million people (6% of the population) were living without access to drinking water and 35.7 million people (17%) without improved sanitation.

The emergency of cholera in Haiti has renewed the global debate on the role of reactive vaccination. Since 2012, OCV has been deployed in several African countries that experienced a cholera outbreak. The effectiveness of two doses of OCV was 87% in an outbreak in Guinea. Simulations suggest that reactive vaccination of people at high risk of exposure would be the most effective use of a limited vaccine stock. As part of contingency plans for *Vibrio cholerae* importations, a tactical use of OCV should be considered as part of an integrated response in specific geographical areas that have a high proportion of people who live in vulnerable conditions, such as rural populations with difficult access to health services (including indigenous people) and urban and peri-urban populations with vulnerability in access to drinking water and sanitation.

Jointly with partners, WHO launched in the second semester of 2013 a global OCV stockpile. This mechanism is managed as a rotating fund by the International Coordinating Group, which already manages similar stockpiles of meningococcal meningitis and yellow fever vaccines for outbreak response. Until June 2014, the International Coordination Group (ICG) accepted 5 country requests for a total 1.4 million doses. The global stockpile thus promises to be a great contribution to the timely deployment of OCV in outbreak settings.

#### **Recommendations:**

- TAG supports PAHO's efforts towards cholera transmission elimination in the Region of the Americas through the integrated action and contingency plans, including the use of OCV where indicated. To this end, efforts to mobilize sufficient resources for maintaining the role of the PAHO Secretariat in the Regional Coalition for Water and Sanitation to Eliminate Cholera in Hispaniola should be pursued.
- TAG reinforces previous recommendations to maintain WASH Advocates as a fundamental pillar to the comprehensive approach towards an overarching goal to eliminate cholera transmission. TAG also reaffirms that vaccination is one of possible short-term actions toward the achievement of the long-term elimination goal.
- Countries should continue cholera surveillance and assess the impact of OCV where used.

## Status of the Documentation and Verification Process of the Elimination of Measles, Rubella, and Congenital Rubella Syndrome

PAHO/WHO defines measles and rubella elimination as the interruption of endemic transmission of these viruses for a period of at least 12 months, in the presence of high-quality surveillance. To confirm elimination of these diseases, countries have to document interruption for a period of at least three years from the last known endemic case. In order to implement the documentation process, an International Expert Committee (IEC) was created and 23 national commissions were established, including one for the French Overseas Departments of the Americas and one sub-regional commission for English-speaking and Dutch-speaking Caribbean countries and territories, including Suriname.

### Progress

In their reports on elimination, the national and sub-regional commissions presented evidence indicating the interruption of endemic transmission of the measles and rubella viruses in their countries and territories including the occurrence of the last endemic measles case in 2002 and the active case searches for the period 2006-2012. This evidence suggested a strong basis for measles elimination in the Region. The evidence—studied by the IEC at its fifth meeting, held in April 2014—is the following:

- a) Member States have documented the last case of endemic transmission of measles and rubella in their countries and territories. Subsequently reported cases were import-associated, according to epidemiological and molecular epidemiology data. The last endemic cases of measles and rubella in the Region occurred on 16 November 2002 and on 3 February 2009, respectively. The last endemic case of congenital rubella syndrome (CRS) was found in a child born on 26 August 2009.
- b) In the period 2009-2013, the Region, on average, met the targets for four of the five epidemiological surveillance indicators (>80%) on a continuous basis (83-91%). The adequate investigation indicator was achieved only in 2011, since in several countries there were difficulties in visiting homes in the 48 hours following reports of suspected cases.
- c) Given the differences among and within countries in terms of sustained achievement of surveillance indicators, 16 of 23 countries with national commissions carried out active institutional and community case-finding over the period 2010-2013, to document the absence of measles and rubella cases in their territories. These countries established criteria for identifying areas for active case-finding, such as municipalities not reporting suspected cases, areas with a heavy flow of tourists or migrants, areas experiencing population shifts, border regions, areas with low vaccination coverage, and the presence of at-risk ethnic groups, among others.
- d) Likewise, 16 of 23 countries with national commissions carried out retrospective searches for suspected cases, using several sources of information. Criteria for selecting the institutions where the searches would be made included level of care and services provided, as well as being located in areas with unreliable notification of suspected CRS cases. No case of CRS was confirmed.

- e) Since the presence of dengue cases in several countries could have masked measles and rubella cases, 15 of 23 countries with national commissions and the Caribbean sub-regional commission tested a percentage of samples from patients with exanthema for measles and rubella in areas where the dengue virus was circulating. The same was done with dengue-negative samples in areas where suspected cases of measles had been reported. None of the processed samples tested positive for measles or rubella.
- f) Genotype D9 was isolated in the last endemic outbreak of measles reported in Colombia and Venezuela in 2002. Since 2003, countries have documented importation of measles cases by identifying viral genotypes. Genotypes D4 and D8, which mainly circulate in Europe, have been found in 88% of outbreaks.
- g) Rubella virus genotype 1C has been identified as endemic in the Americas. From 2006 to 2009, genotype 2B was isolated in outbreaks reported in three countries and is also considered endemic in the Region. For the period 2009-2013, reported genotypes 1E, 1G, 1J, and 2B have been linked to imported cases.
- h) From 1994 to 2013, nearly 500 million people  $\leq 40$  years of age were vaccinated in catch-up, follow-up, and speed-up campaigns. To complement the cohort analysis, 18 of 23 countries with commissions estimated the accumulation of susceptible individuals, prior to defining the target population for follow-up and speed-up campaigns.

At the fifth meeting of the IEC, Brazil presented the current epidemiological situation of the sustained measles outbreak affecting the states of Ceará and Pernambuco. After updating the figures through the weekly measles bulletins, the number of cases reached 424 confirmed cases for the period 2013-2014.<sup>2</sup> The date of rash onset was 19 March 2013 for the first case and 10 June 2014 for the most recent confirmed case. In addition, 53 suspected cases remain under investigation; rash onset of the last suspected case is 1 July in Ceará. The cases are distributed in 24 of 185 municipalities in Pernambuco and 13 of 184 municipalities in Ceará. Children under 1 year of age is the group most affected by this outbreak (43%); however, 100 cases in adults (>15 years) have been confirmed. Genotype D8 has been identified. The country has conducted a vaccination campaign aimed at children under 5 years of age in the affected states and has strengthened epidemiological surveillance as part of the attempt to interrupt this outbreak. TAG expresses concern that the measles outbreak in Brazil has persisted for over 15 months and that cases are still under investigation. While all documentation previously presented to the IEC pointed towards interruption of endemic measles circulation, the current outbreak is not consistent with elimination and must be urgently stopped. To this end, TAG is aware that both PAHO and the IEC stand ready to assist the government of Brazil in successfully interrupting the measles virus transmission in the country.

Global circulation of measles and repeated outbreaks represents a continuous risk of virus reintroduction into the Americas. The recent large outbreaks in Ecuador, Quebec, Brazil and United States have illustrated this real risk. TAG has previously stated that there is no room for complacency in order to maintain the achievements of elimination.

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<sup>2</sup> Data as of epidemiological week 24, 2014 (29 June – 5 July).

**Recommendations:**

- TAG recommends that the PAHO Secretariat review, with the Brazilian authorities, the epidemiological data and the outbreak response in order to identify opportunities to halt the epidemic as soon as possible.
- To this end, TAG urges Brazilian authorities to present the most updated data and outbreak response to both the TAG and IEC members.
- TAG suggests the Brazilian government consider PAHO's availability and readiness to provide any type of assistance to interrupt the measles virus transmission in the country.
- PAHO Secretariat should lead a further in-depth examination of the epidemiology of and response to recent outbreaks to better understand transmission patterns and age-distribution of cases, use of MR vs. MMR vaccines in outbreak response, the usefulness of dose 0 at 6 months of age in addition MMR1 at 12 months of age and MMR2 at 18 months of age during outbreaks.
- All countries need to maintain their capacity to respond rapidly and decisively to outbreaks. In order to anticipate the spread of an outbreak, thorough outbreak investigation is critical in order to define geographical areas and age ranges to be targeted. Outbreak responses must be aggressive and timely to halt secondary transmission.
- All countries should also review their measles/rubella surveillance performance and vaccination coverage levels to identify areas of vulnerability. Specifically and within the context of the 2014 FIFA World Cup, countries should implement additional surveillance actions (i.e., active searches) to document the absence of measles and rubella cases.
- TAG reemphasizes previous recommendations that coverage of at least 95% with 2 doses of measles-containing vaccines in all districts and in all countries is needed to maintain elimination. If 95% coverage is not reached with two doses, countries should continue to conduct periodic follow-up campaigns.
- TAG reissues its 2013 recommendation to lower the age for the second MR-containing vaccine dose to 18 months and use school entry requirements as a platform to monitor MR-containing vaccine vaccination status.

## Update on Pertussis Vaccination

The TAG has made several recommendations regarding pertussis surveillance and vaccination in the last four years. One of these recommendations was that countries should not change the whole-cell vaccine from routine vaccination against pertussis to acellular vaccines, because of evidence suggesting the shorter duration of the immunity conferred by the acellular vaccine.

In November 2012, SAGE expressed concern about the apparent resurgence of pertussis in some industrialized countries despite high vaccine coverage with acellular pertussis (aP) vaccines, which in some settings was associated with an increase in infant pertussis deaths.

With the objective of reviewing the most recent evidence about aP vaccine effectiveness, SAGE established a working group that reviewed the data of 19 developing and industrialized countries from various regions around the world that showed high vaccination coverage with the whole-cell pertussis vaccine (wP) or the aP vaccine.

Given the natural periodicity of pertussis, disease resurgence was defined as a larger burden of disease than expected when compared to previous cycles in the same setting.

### ***Main conclusions of SAGE pertussis working group:***

- The vaccination against pertussis is highly effective in reducing disease caused by *Bordetella pertussis*, with a large decline in overall global incidence and mortality compared with the pre-vaccination era in both wP- and aP-using countries.
- To date, there is no evidence of a widespread global resurgence of pertussis. There is however evidence that resurgence has occurred in 5 of the 19 countries reviewed, 4 of which were exclusively using aP vaccines. The increased number of cases in 1 country using wP vaccine was considered to reflect factors other than the use of this vaccine, such as surveillance, laboratory methods, and low vaccine coverage in some areas.
- Recent modeling studies, as well as data from a baboon model, supported the hypothesis that wP to aP vaccine transition may be associated with disease resurgence.
- Although the reasons for the resurgence were found to be complex and varied by country, SAGE concluded that the shorter duration of protection and likely reduced impact on infection and transmission conferred by aP vaccines play critical roles.
- The influence of changes in circulating pertussis strains on the effectiveness of aP or wP vaccines was not found to contribute to observed country level resurgence.
- Licensed aP vaccines have lower initial efficacy, faster waning of immunity, and possibly a reduced impact on transmission relative to currently internationally available wP vaccines, as aP vaccines induce a different type of immune response, and are less effective in clearing mucosal infections.
- Surveillance and modeling data suggest that the use of aP vaccines may result in a resurgence of pertussis after a number of years and might lead to an increased risk of death in young infants compared with programs using wP. The magnitude and delay for

this resurgence to occur are difficult to predict, given the many factors that intervene such as vaccine coverage, natural immunity, vaccine type, schedules, etc.

- Recent evidence suggests that maternal immunization with aP during pregnancy is safe and highly effective in protecting infants from pertussis and that it may have a high impact on morbidity and mortality in infants too young to have been immunized. This conclusion does not extend to wP vaccines, given the absence of immunogenicity and efficacy data in pregnant women and concerns regarding potential higher reactogenicity in adults.
- Vaccination of pregnant women is considered likely to be the most cost-effective complementary strategy to prevent pertussis-associated infant mortality.

### ***SAGE Recommendations***

All children should be immunized against pertussis, with the goal of maintaining high coverage, as minor reductions can lead to an increase in incidence.

The risk of resurgence associated with the use of aP vaccines for primary immunization, including increased disease in infants, compared with use of wP, indicates that countries where only a limited number of pertussis doses are used/affordable should continue to use wP vaccines for primary pertussis early infant vaccination. Thus the switch from wP to aP vaccines for primary infant immunization should only be considered if large numbers of doses (including several boosters) can be included in the national immunization schedules; this has substantial cost implications given the much higher cost of aP vaccines and higher number of doses required.

Countries may consider the immunization of pregnant women with 1 dose of Tdap (in the 2<sup>nd</sup> or 3<sup>rd</sup> trimester) in addition to routine primary infant pertussis vaccination in countries or settings with high infant morbidity/mortality due to pertussis.

SAGE emphasized the importance of efforts to improve surveillance of disease burden particularly in developing countries, and assessment of impact of infant immunization, with particular focus on fatalities in infants <1 year of age.

### **Recommendations:**

- Although both available pertussis vaccines (aP and wP) elicit a good immune response, evidence suggests aP has a short-lived duration of protection. As such, countries should give preference to the use of wP containing vaccines. Countries using current vaccination schedules with whole-cell pertussis vaccines should continue to do so and countries using aP should actively monitor the risk that waning immunity poses to the population.
- PAHO should engage with partners, including WHO, in discussions with industry to advocate for the research and development of improved pertussis containing vaccines.

- Countries should ensure homogenous vaccination coverage  $\geq 95\%$  with 3 doses of pertussis-containing vaccines in children aged  $<1$  year; and encourage timely initiation and completion of the schedule. Coverage attained with the 4<sup>th</sup> dose of the DPT vaccine should be the object of careful recording, monitoring, reporting and evaluation.
- All countries should continue strengthening pertussis surveillance to better monitor the epidemiology of the disease. Also, countries should continue assessing the quality of their laboratory diagnostics and 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.
- Every pertussis outbreak should be thoroughly investigated to improve the understanding of the current epidemiology of the disease in the Region of the Americas.
- The response to outbreaks of whooping cough should include lowering the age for initiating vaccination to 6 weeks and vaccinating pregnant women only in areas affected by the outbreaks. Currently, there is no evidence for TAG to recommend routine vaccination of pregnant women.

## Update on the PAHO Revolving Fund

For 35 years, the PAHO Revolving Fund (RF) has been one of the cornerstones of success of the immunization programs in the Region, in terms of the elimination and control of vaccine-preventable diseases and the rapid and sustainable introduction of new vaccines. In 2013, on behalf of 41 countries and territories, the RF acquired 46 different vaccine presentations, as well as syringes and cold chain equipment. A total of 1,335 purchase orders, with a consolidated value of \$495 million, were also placed, with more than 95% of funds from coming national budgets.

The countries and territories that participate in the RF have strongly expressed that it is critical to strengthen the management of the Fund and to safeguard its principles, including solidarity, Pan Americanism and equal access, in order to protect the achievements, progress and financial sustainability of immunization programs. However, the RF faces significant challenges with respect to the context of the vaccine market, in terms of the price and supply of some biologicals.

In order to strengthen the management of the RF, during the 52<sup>nd</sup> Directing Council in October 2013, Member States recognized the strategic importance of the RF and approved increasing their contribution from 3.5% to 4.25% (while maintaining the 3% RF capitalization rate) in order to increase the financial sustainability of this mechanism, while also ensuring greater efficiency and service in favor of countries and territories.

Similarly, during the same Directing Council, a resolution was passed that endorsed the principles of the RF and requested that PAHO continues administering this mechanism, without exception, in a way that respects its principles, terms and conditions, which that have contributed to the successes of the immunization programs in the Region. In particular, offering all countries vaccines at a single price and ensuring that is the lowest available. Since the principles of the RF were ratified however, some partners and vaccine producers have promoted- with even greater intensity- a differential pricing policy; in other words, they have promoted that countries, within the Revolving Fund and in other regions, pay vaccine prices according to their per capita income (Gross National Income – GNI per capita).

Regarding vaccine supply, the RF is faced with situations of limited or sensitive supply for four vaccines: yellow fever, Tdap, varicella and MMR. The global production capacity of the yellow fever vaccine continues to be insufficient. Because of this, a WHO/UNICEF/PAHO working group was established to prioritize the allocation of the limited supply.

The global demand for Tdap and varicella vaccines is increasing faster than production capacity, creating conditions of scarcity. In addition, reducing inventories in progress and long production cycles for these vaccines affect the availability to meet demands from countries that are not planned in advance.

With regard to measles-containing vaccines (MR and MMR), the global supply is inconsistent. Of the four prequalified producers, one has 80% of global production capacity, two have production difficulties and high prices, and one is stopping. The growing global demand for these vaccines can affect the timely supply, if countries in the Region do not plan their needs precisely and in advance.

To address these challenges, the RF has made improvements to its tools for supporting countries in their timely, long-term demand planning, as well as in their plans for vaccine introduction.

**Recommendations:**

- TAG reaffirms its recognition of the RF as a pillar in the progress and success of country immunization programs in the Americas. In turn, the TAG acknowledges the support that countries and territories provide to the RF.
- The TAG continues to recommend that countries ensure the development of increasingly accurate demand forecasts and with greater long-term visibility. The PAHO RF should support countries in the process of planning and monitoring.
- TAG continues to support other regional pooled procurement initiatives, such as the ongoing discussion in the Eastern Mediterranean Region of the World Health Organization.

## Update on Immunization Data Quality and Electronic Immunization Registries

Evidence supports the fact that more effective immunization coverage monitoring leads to better coverage. Latin America is a global leader in regional and country-led initiatives in the area of immunization data use and quality. Many countries in Latin America are rapidly advancing in the development and implementation of national electronic immunization registries (EIRs).

Immunization data quality, defined in practical terms as data that effectively reflects the reality it is meant to describe, is considered a priority for countries of the Americas and PAHO. The issue of immunization data quality was first discussed formally by Ministers of Health in 2002, in the context of a regional Resolution approved by PAHO's Sanitary Conference (CSP26.R9). That same year, PAHO's TAG on Vaccine-preventable Diseases put forward recommendations on data quality urging countries to regularly and systematically assess the quality of immunization data, within the context of regular ongoing supervisory activities. TAG also urged countries to strengthen data analysis capabilities including the identification of high-risk municipalities and the causes of low coverage, leading to the development of micro-plans to correct identified problems. Moreover, it called for the dissemination of assessment tools, for local adaptation and use.

TAG has since reinstated its original data quality recommendations, adding recommendations not only to assess data quality, but also to develop and implement work plans to follow-up on the monitoring system weaknesses detected. In 2009, TAG added a recommendation regarding the importance of having the EPI be actively involved in health surveys collecting vaccination coverage data. Also in 2009, TAG first issued a recommendation on EIRs, in the context of improving data quality, urging countries using EIRs to share experiences and lessons learned. Additional EIR recommendations were added in 2011 and in 2013, as more and more countries began developing and implementing EIRs. These recommendations call for coordination with other actors, system interoperability, EIRs that take into account the needs of the vaccinators, more monitoring and evaluation, and exploring using innovative mHealth technologies.

In the global context, since the inception of the DoV initiative and the implementation of the GVAP, endorsed by all WHO Member States in 2012, monitoring and evaluation have been at the forefront of the global immunization agenda. The progress report on GVAP presented to the World Health Assembly in 2014, highlighted issues related to the availability and quality of the data needed to monitor the achievement of GVAP goals and strategic objectives. During the 2014 World Health Assembly (WHA), several countries expressed their concern about immunization data. Countries from the Americas also expressed their awareness of the issues related to immunization data quality, and at the same time were able to share the steps they are taking to improve data quality and immunization monitoring.

SAGE discussed data issues with a focus on the WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) in 2011. More recently, SAGE has emphasized the importance of improving data quality in order to better monitor the GVAP, but always stressing the importance that data has for managerial decisions at all levels, starting with health facilities.

Developing and maintaining good practices on data collection, aggregation and reporting, form archiving and analysis for decision-making is increasingly challenging. Primarily because more and more vaccines are added to vaccination schedules, the same personnel often has to deal with the delivery of more and more health interventions to more users in health facilities, and data collection needs multiply. In spite of these challenges, progress on improving immunization data quality and using that data for decision-making at all levels has been remarkable in Latin America over the last twelve years.

In this TAG session, the progress report on data quality and EIRs focused on activities done to improve data quality and use at the local level, data quality assessments, vaccination coverage surveys, and the implementation and development of EIRs. It presented work done on data quality assessment tools as part of a toolkit for coverage monitoring of integrated interventions targeting children and introduced the recently launched project “Improving Data Quality on Immunization” (IDQi). Finally, some important open questions were shared and PAHO’s vision and next steps on data quality and EIRs were presented.

Some details on the work on data quality and use, and EIRs in Latin America are provided herewith:

#### ***Data quality and use at the local level***

An important aspect of the work in immunization data quality has focused on where the data are generated: the local level. Recommendations have revolved around encouraging health care workers, the vaccinators, to use the data they collect to monitor the achievement of coverage goals and their drop-out rates, and to track and contact defaulters. Supervisory visits that include reviewing data on doses given, monitoring proper data recording practices, using paper registries or ticker-files to track defaulters, in addition to field verification of the vaccination status of the community, are strongly promoted. Work has also been done to promote the quality and proper use of vaccination cards.

#### ***Data quality assessments and follow-up***

Formal immunization data quality assessments, implemented by PAHO hand-in-hand with countries, using an adaptation of the WHO’s Data Quality Self-assessment (DQS), have been very useful in making immunization data quality and use an important component of the EPI. The first DQS in Latin America was conducted in Costa Rica with PAHO support in 2005. To date, over twenty countries have conducted a data quality assessment. Measurable improvements have been seen in countries that have repeated such assessment. Furthermore, the inclusion of concrete recommended activities following these assessments into annual or multiyear

immunization plans of action have resulted in increased visibility and heightened likelihood of implementing the recommendations.

### ***Coverage surveys***

Most surveys assessing immunization coverage rates in Latin America and the Caribbean are the Demographic and Health Surveys (DHS) and UNICEF's Multiple Cluster Indicator Surveys (MICS). To ensure that the data resulting from these and other similar surveys are useful to EPI managers, in 2009, TAG issued a recommendation urging immunization programs to be aware of the conduct of such surveys in order to ensure that questionnaires are adequate and interviewers are properly trained to assess vaccination status, and that the results are internally consistent between biologicals. EPI managers have been engaged with survey planning teams and PAHO, in collaboration with the US CDC, has been collaborating with countries to conduct secondary analyses focusing on vaccination timeliness, simultaneity, potential missed opportunities and related factors. PAHO has also recently supported surveys that seek to answer specific questions, in addition to coverage rates: Haiti (2009 and 2012), Paraguay and Venezuela (2011), El Salvador (2011-2012) and Bolivia (2013). The latter also included an operational study component to assess validity of maternal recall and to assess card quality (from pictures taken in the field) and data reliability between sources; analysis is ongoing.

### ***Electronic Immunization Registries***

With the increased availability of information and communication technologies, as well as connectivity in all countries over the last few years, countries have been developing and implementing EIRs. If well implemented, EIRs can facilitate monitoring coverage and implement tailored strategies aimed at increasing coverage. They can also help optimize the workflow and facilitate defaulter tracking, not only improving data quality and use, but also making immunization programs more efficient.

PAHO has facilitated experience exchanges between countries mainly through visits, virtual seminars, and face-to-face meetings. A landmark workshop to discuss issues related to the development and implementation of EIRs was held in Colombia in 2011 and a follow-up Immunization Registry workshop, with Latin American countries and selected GAVI-eligible countries from other regions, took place in Brasilia in November 2013. From this work, best practices and lessons learned on EIR development, implementation and use are being compiled. Much remains to be done in terms of EIR Monitoring and Evaluation (M&E). In May 2014, a DQS conducted in Panama included a module on EIR. This EIR evaluation module was recently developed by PAHO with support from partners. It includes questions to describe the registry's scope, the software's architecture, the EIR functionalities, the regulatory and legal context, issues of maintenance and sustainability; human resources; level of implementation and future plans. Questions on availability of adequate hardware (i.e. computers), Internet access, infrastructure, human resources and technical support, adequate use of the EIR and perceptions of EIR users (EPI and data entry clerks) were added to the DQS quality tools. The tool was useful and it will continue to be used and improved.

Finally, in order to move forward with technical cooperation on data quality and EIR development, implementation and M&E, PAHO has started implementation of project IDQi, which seeks to raise awareness of, interest in and commitment to select strategies in order to better track facility performance via immunization coverage monitoring. The IDQi project also seeks to improve follow-up of un/under-immunized individuals and foster linkages between coverage and supply chain data. Its expected outcomes include launching a virtual library of data quality best practices drawn from at least 3 case studies, launching a live toolkit that helps countries effectively initiate and/or improve embedded monitoring, and another toolkit that helps countries decide whether, when and how to introduce and/or expand EIRs. It also aims to raise awareness in 50 countries of all IDQi tools by 2016, 60% of which should be outside of PAHO. A TAG Member has been invited to be part of the IDQi project Advisory Group to help ensure that the project implementation is aligned with TAG recommendations.

**Recommendations:**

- TAG endorses the work being done in the Region in the area of immunization data quality and electronic immunization registries, as these efforts are in line with the GVAP, and reiterates all of its recommendations from previous years.
- TAG agrees that immunization data quality should be approached from several fronts, while always keeping the local level as the foundation for any efforts.
- TAG encourages the continued exchange of experiences between countries.

## Vaccination with Pneumococcal Conjugate Vaccine in Adults

Pneumococcal pneumonia and other diseases caused by *Streptococcus pneumoniae* (*Spn*) 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. The burden of pneumonia disease in adults is greater in adults  $\geq 65$  years of age as has been seen in the United States, Argentina, and Brazil. In addition, the burden of this disease has increased due to the number of individuals with chronic diseases or infected with human immunodeficiency virus (HIV), and the increased age 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.

The 13-valent pneumococcal conjugate vaccine (PCV) is prequalified by the WHO and licensed for ages  $\geq 50$  years in several countries. Preliminary results of placebo-controlled double-blind clinical trials of PCV13 vaccine, carried out in over 85,000 people aged  $\geq 65$  years, showed efficacy in pneumonia reduction (CAPiTA study). However, to date, the final results have not been published.

As demonstrated with PCV7 vaccine, recently published studies demonstrate a reduction in invasive pneumococcal disease (IPD) and pneumonias in adults in the United States with the introduction of PCV13 in the vaccination schedule for children. In other industrialized countries, the incidence of IPD has decreased sharply with the introduction of pneumococcal conjugate vaccines, including other age groups that are not the primary vaccination target group, due to the herd immunity effect these vaccines provide.

Given that data on the herd effect is limited in low and medium income countries, it is difficult to predict the impact of pneumococcal conjugate vaccines introduced into the childhood vaccination schedule on the reduction of pneumonia, IPD, and serotype replacement in LAC. However, a study in Brazil demonstrates the effect of PCV10 on the reduction of child carriers. Several issues need to be considered in evaluation of the herd effect:

- Availability of surveillance data in the adult population (most LAC countries do not have this information).
- At least three years since the introduction of PCV in children.
- Data on colonization rates in children. In LAC, rates are around 45%.

- Strength of pneumococcal infection transmission. Socio-demographic factors such as overcrowding may facilitate pneumococcus transmission from a colonized person to others.
- Individual immunological response to the vaccine may be influenced by factors such as malnutrition, immunological status, and others.
- PCV vaccination coverage in children. PCV vaccine coverage in LAC is high in general.
- Vaccination schedules adopted by the countries (3+1; 3+0; 2+1).

To date, 27 countries and territories in the Region have introduced pneumococcal conjugate vaccines (PCV10 or PCV13); however, there is still no evidence of herd effect in LAC countries.

More recently, PCV13 immunogenicity studies have been conducted in adults. These studies have demonstrated good immunogenicity, especially for the serogroups included in the vaccine, both in healthy adults and in high-risk patients. The available data indicate that the high-risk population has a greater probability of developing pneumococcal disease and death.

In regard to cost-effectiveness, there are few studies on the cost-effectiveness of PCV13 vaccine in adults in LAC. Cost-effectiveness analyses in LAC will depend on future studies based on data on the adult disease burden, direct local medical costs, vaccine costs, herd effect, and data on efficacy of PCV13 in adults.

Countries should consider programming and logistical aspects of the introduction of a new vaccine in the immunization program, considering recent prior experiences with the introduction of other new vaccines.

PAHO organized a working group in WDC, on 2-3 June 2014 in order to discuss the topic of adult vaccination with the 13-valent pneumococcal conjugate vaccine (PCV13) as a public health policy in Latin American and Caribbean countries (LAC). The conclusions of the group discussion were presented to the TAG.

#### **Recommendations:**

- TAG endorses the recommendations of the working group, including:
  - The introduction of pneumococcal conjugate vaccines in children continues to be the priority for reduction of pneumococcal disease.
  - Introduction of PCV13 vaccination for healthy adults into immunization programs will depend on the results of studies of efficacy, cost-effectiveness, and herd effect.
  - Countries that have already introduced the 23-valent polysaccharide vaccine for use in adults could use the sequential schedule (conjugate-polysaccharide) for high-risk adults\*.
  - Countries that do not use pneumococcus vaccine in high-risk adults\* and consider vaccination of this population a priority could include PCV13 in their vaccination schedules, based on immunogenicity studies.
  - Implementation or strengthening of epidemiological surveillance of pneumonias and IPD in adults is a priority for countries.

- Countries that have already introduced PCV vaccines for children should spell out mechanisms to measure the impact of vaccination on other age groups (herd effect).
- TAG encourages innovative surveillance and assessment approaches to better understand the preventable burden of pneumococcal disease in adults. Interaction with influenza surveillance networks should be further explored.
- Countries should seek to improve PCV vaccination coverage rates in children.

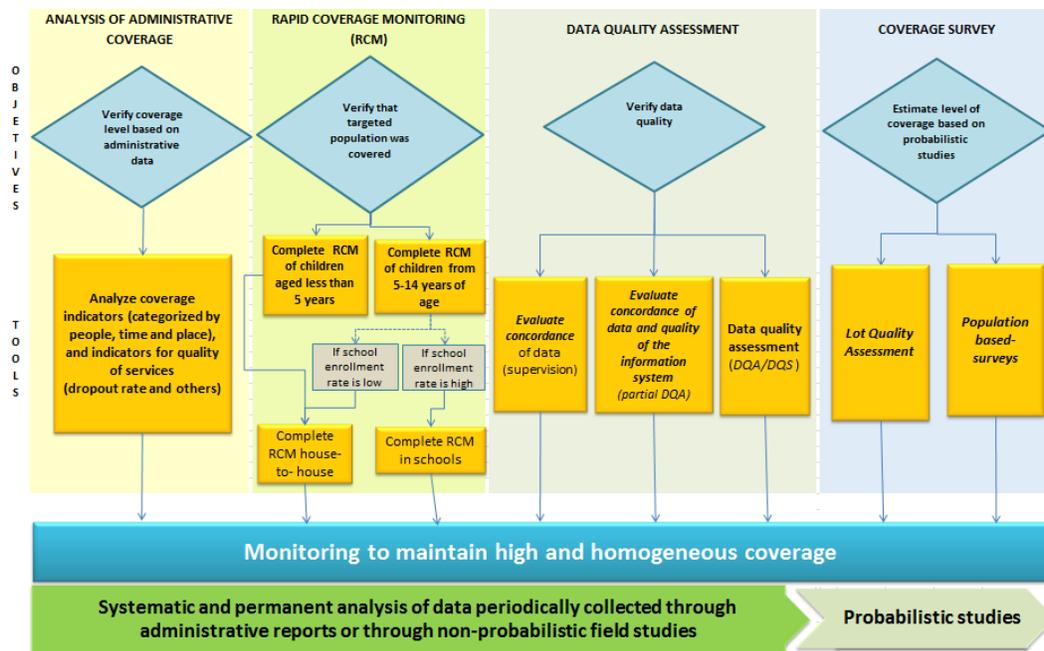
\* Adults in high risk groups are adults  $\geq 50$  years of age, with the follow conditions: cerebrospinal fluid leak, cochlear implant, sickle cell disease/other hemoglobinopathy, congenital or acquired asplenia, immunocompromised persons, congenital or acquired immunodeficiency, human immunodeficiency virus infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma , Hodgkin’s disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant, and multiple myeloma. This is a special recommendation for individual clinical decision-making.

## Tools for Improving the Effective Management of Immunization Programs at all Levels

In the context of high national vaccination coverage, reaching unvaccinated people requires a good understanding of the profile and location of vulnerable populations as well as the reasons they give for not initiating or completing the vaccination schedule. Thus, in 2002, TAG recommended that countries build data analysis capacity, including identification of high-risk municipalities and the causes of low coverage, and that the Organization develop and disseminate tools for their local adaptation and use. These recommendations were revisited in 2010 and 2013, and the Directing Council of the Pan American Health Organization recommended that the Director provide technical support to the Member States for evidence-based decision-making and for strengthening immunization programmatic and operational capacity.

In order to respond to the challenge of promoting systematic data analysis for immunization decision-making and programmatic strategy development, PAHO has created tools to 1) identify missed opportunities for vaccination that could make it easier to increase immunization service coverage; 2) systematize and facilitate monitoring of immunization data (and other interventions administered concomitantly with immunization) from the local level (figure below); and 3) integrate cost analysis into the planning and budgeting process.

Among the next steps, PAHO will continue to systematize the tools that countries have been using to provide local levels with guidance on data analysis to identify the characteristics of unvaccinated people and develop efficient strategies to reaching these populations. In an upcoming EPI evaluation, PAHO will integrate these three management and operational tools to help identify the most efficient strategies to employ in the micro planning and strategic planning processes for reaching the unvaccinated.



### Recommendations:

- TAG recognizes these tools for EPI are of great value for making informed decisions at the local, intermediate and national level.
- TAG encourages countries to test and adopt the tools proposed by PAHO, as well as document how these tools contribute to improved management of the program.