

# Immunization Newsletter

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## XXIV Meeting of the Technical Advisory Group on Vaccine-preventable Diseases



Participants at the XXIV Meeting of PAHO's Technical Advisory Group on Vaccine-preventable Diseases (TAG), July 2017. Credit: David Spitz, PAHO/WHO.

The XXIV Meeting of the Technical Advisory Group (TAG) on Vaccine preventable Diseases of the Pan American Health Organization (PAHO) was held in Panama City, Panama on 12-14 July 2017.<sup>1</sup> The slogan for the meeting was “40 years and counting,” selected in celebration of the 40th anniversary of the Expanded Program on Immunization (EPI), which was created in 1977.

The objectives of this meeting included reviewing the progress on several initiatives focused on controlling and eliminating vaccine-preventable diseases (VPDs) and issuing recommendations on ways to address the many challenges faced by national immunization programs in the Americas. The topics discussed during the meeting, *Plan of Action for Sustaining Measles, Rubella and Congenital Rubella Syndrome Elimination in the Americas 2018-2023*<sup>2</sup> and *Plan of Action on Immunization: Midterm Review*<sup>3</sup> will be presented at the Region's upcoming Pan American Sanitary Conference in September 2017.

Panama's Ministry of Health opened the meeting and expressed their happiness to host the event, recognizing how the meeting will greatly benefit public health at the national, regional and global levels. The importance of Panama's EPI was also mentioned, as it provides the country's population with free and equitable access to 23 vaccines, including to people in difficult-to-reach geographic and indigenous areas. The successes of Panama's EPI, which can be attributed to its strong, committed healthcare staff, and the high acceptability of vaccines by its people, can be seen as an example for other countries, but also as contributing to the success of the Region as a whole. PAHO's Assistant Director, Dr. Francisco Becerra, and TAG chair, Dr. Peter Figueroa followed the speech from Panama by welcoming participants to the meeting. ■

<sup>1</sup> The topics presented in this issue of the Immunization Newsletter were marked “For decision” at the 2017 TAG Meeting. A complete list of topics and recommendations can be found in the Final TAG 2017 Report, accessible at [www.paho.org/immunization/TAG-Reports](http://www.paho.org/immunization/TAG-Reports)

<sup>2</sup> Document CSP29/8, available at <http://bit.ly/PlanofActionMRCRS>

<sup>3</sup> Document CSP29/INF/7, available at <http://bit.ly/RIAPmidterm>

### IN THIS ISSUE

- 1 XXIV Meeting of the Technical Advisory Group on Vaccine-preventable Diseases
- 1 Update on Polio and Progress towards the Final Phase of Eradication
- 4 Mid-term Report on Achieving the Goals of the Regional Immunization Action Plan (RIAP)
- 6 Meningococcal Vaccine Use in the Routine Immunization Program
- 7 Plan of Action for Sustaining the Elimination of Measles and Rubella in the Americas
- 8 Letter from Dr. Fernando Muñoz, winner of the PAHO Immunization Award 2017, thanking PAHO Director Dr. Carissa Etienne

## Update on Polio and Progress towards the Final Phase of Eradication

### Global update

Countries worldwide have made important progress toward their commitments to global polio eradication. Each day more children in the remaining endemic countries (Afghanistan, Nigeria, and Pakistan) are fully protected. Along the Pakistan-Afghanistan border, considered a poliovirus reservoir, the number of zero-dose acute flaccid paralysis (AFP) children (a key surveillance indicator) has continued to fall from 24% in 2014 to 2% in 2016. In Nigeria, 95% of AFP cases aged 6–59 months received more than four oral polio vaccine (OPV) doses. In 2016, countries reported only 37 AFP cases, the lowest number ever. As of 4 July 2017, only six cases of wild poliovirus (WPV) have been reported, compared to 19 cases reported by the same date in 2016. However, these three countries have areas that are inaccessible due to insecurity, where WPV is still endemic. For example, in August 2016 in Nigeria, four WPV1 strains were isolated from AFP cases identified among internally displaced families in three districts of the Borno State. This was a major setback for global eradication efforts. In addition, the circulation of vaccine-derived poliovirus (cVDPV) continues to occur. In 2016, five cVDPV cases were reported, while as of 4 July 2017, 28 cases of cVDPV have already been reported, compared to three cases by the same date in 2016.

### Regional update

In accordance with the Polio Eradication and Endgame Strategic Plan (PEESP), between 2015 and 2016, all countries in the Region that exclusively used the trivalent oral polio vaccine (tOPV), introduced one dose of the inactivated poliovirus vaccine (IPV). Subsequently, by April 2016, the 36 countries that were still using OPV in their routine schedule switched from tOPV to bivalent

See **POLIO** on page 2

**POLIO** continued from page 1

oral polio vaccine (bOPV). After the switch, all 36 countries completed supervision in 100% of warehouses and vaccination clinics and submitted reports, which were validated by both National Certification Committees (NCCs) and the Regional Certification Commission (RCC).

Over the last 15 years, regional vaccination coverage for three doses of polio vaccine (polio-3) has ranged from 90-94%. However, the Region has not met its goal of  $\geq 95\%$  polio-3 coverage because too few countries have met the target at the national level. At the sub-national level, vaccination coverage is not uniform among municipalities.

The ability to detect and respond to outbreaks depends on the quality of polio surveillance, and AFP surveillance is the gold standard for monitoring the absence of WPV and cVDPV circulation. In the last five years, the Region has achieved a notification rate of  $\geq 1$  AFP case per 100,000 children aged <15 years; the percentage of cases with adequate stool samples obtained within 14 days of the onset of paralysis, which should reach at least 80%, has ranged from 73-79% in the 10 years and is 75% in the last 52 weeks<sup>5</sup>. The percentage of AFP cases investigated within 48 hours of notification, which should reach at least 80%, has ranged between 61-91%, and is 80% in the last weeks<sup>5</sup>. In 2016, only Nicaragua and Paraguay have met these three indicators; in the last 52 weeks, only Paraguay achieved all three indicators.

Between 2012-2016, only four AFP cases were classified as polio-compatible. However, upon analyzing AFP data on a case-by-case basis, 568 AFP cases were discarded without adequate stool samples or follow-up to check for residual paralysis or sequelae. According to PAHO's Polio Field Guide (2006)<sup>6</sup>, cases without adequate samples and follow-up should be classified as compatible cases and should be considered failures of the surveillance system.

### Polio risk assessment

It is important for countries to know the risks of importation of WPV and of a cVDPV event. As such, continued vigilance in the Region is needed to ensure high vaccination coverage and to improve the quality of AFP surveillance for timely detection and response to outbreaks. With support from the RCC, PAHO developed a risk analysis methodology to evaluate the risk of poliovirus importation to the Americas.

The methodology proposes four components for assessment: i) immunization coverage, as a proxy for the level of immunity in the population; ii) AFP surveillance; iii) outbreaks, including history of cVDPV or any other VPD and availability of an outbreak response plan; and iv) others that include population and health-system specific factors that could influence national capacity to detect and respond to WPV importations or cVDPV events.

The analysis was recently conducted and included collecting and analyzing pre-existing information from the PAHO-WHO/UNICEF joint reporting form (JRF), PAHO-WHO's Integrated Surveillance Information System (ISIS) and PAHO Health Situation in the Americas: Core indicators. Results of this assessment showed that three countries were at very high risk for polio importations, five countries were at high risk, nine countries were at medium risk, and three countries were at low risk (**Table 1**). To date, 31 countries have submitted plans to PAHO for the detection and response to poliovirus events or outbreaks.

**Table 1. Risk Assessment for poliovirus importation into countries of Latin America; risk scores are classified as very high (score $\geq 9$ ), high (8-9), medium (6-7) and low ( $\leq 5$ )**

| No. | Country            | Score |
|-----|--------------------|-------|
| 1   | Guatemala          | 9.8   |
| 2   | Haiti              | 9.6   |
| 3   | Venezuela          | 9.2   |
| 4   | Brazil             | 8.2   |
| 5   | Dominican Republic | 8.1   |
| 6   | El Salvador        | 8     |
| 7   | Peru               | 7.9   |
| 8   | Ecuador            | 7.6   |
| 9   | Paraguay           | 7.4   |
| 10  | Panama             | 7.1   |
| 11  | Colombia           | 7.1   |
| 12  | Argentina          | 7     |
| 13  | Honduras           | 6.9   |
| 14  | Bolivia            | 6.5   |
| 15  | Chile              | 6.2   |
| 16  | Nicaragua          | 6.1   |
| 17  | Costa Rica         | 6     |
| 18  | Uruguay            | 5.6   |
| 19  | Cuba               | 5.5   |
| 20  | Mexico             | 4.9   |

### Global containment status

Progress has been made to contain type 2 poliovirus since the publication, in December

2014, of the WHO *Global Plan of Action to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use (GAPIII)*.

As of 1 May 2017, 175 countries and territories reported that they no longer had wild or type 2 vaccine-derived poliovirus, 18 reported that they did, and 12 were completing reports. Thus far, 30 countries have designated 77 poliovirus-essential facilities (dPEF) to retain type 2 polioviruses, but some still have to nominate the National Authority for Containment (NAC) that will be responsible for certifying that these facilities meet the containment requirements described in GAPIII.

The Containment Advisory Group (CAG) is developing guidelines to help facilities to identify samples that are likely to harbor type 2 polioviruses, which will include recommendations on their destruction or secure handling. To support Phase II implementation, WHO and its Regional Offices have raised awareness about containment and strengthened national capacity by training the staff of national authorities for containment and poliovirus-essential facilities about GAPIII implementation and certification.

### Regional containment status

Aligned with GAPIII, the Regional Action Plan for poliovirus containment is being implemented in three phases linked to the milestones in the Global Polio Eradication Initiative (GPEI). The Regional plan is conducted in 44 countries and territories following WHO and RCC guidelines, and with PAHO technical support. A total of 44 polio containment coordinators have been designated in the Region.

In June 2017, the RCC reviewed 19 of 23 expected reports corresponding to 18 country reports and one report from the Caribbean sub region. All countries have submitted at least one phase I progress report on GAP III: Containment of WPV2 / VDPV2 / OPV2 / Sabin2. The RCC has fully validated three country reports for the survey process, inventory, and identification of infectious and potentially infectious material with WPV2/VDPV2/OPV2/ Sabin2, 18 reports for materials infectious and potentially infection with WPV2/VPDV2, and 13 reports report for material infectious with Sabin 2.

Six countries of the Region have designated 31 Poliovirus Essential Facilities (dPEFs)—two

<sup>4</sup> Last 52 weeks, ending in epidemiological week 26 (1 July 2017).

<sup>5</sup> Poliomyelitis Eradication Field Guide (2006), available in English and Spanish at [www.paho.org/hq/index.php?option=com\\_content&view=article&id=787&Itemid=1617&lang=en](http://www.paho.org/hq/index.php?option=com_content&view=article&id=787&Itemid=1617&lang=en)

**POLIO** continued from page 2

in Brazil, four in Canada, one in Cuba, three in Chile, one in Mexico, and 20 in the United States. Only two of these countries have nominated a National Authority for Containment (NAC). A regional training workshop designed for GAPIII auditors to support NACs in their efforts to implement Containment Certification Scheme (CCS) was held in February 2017. Each dPEF should submit applications for the certification process to the NACs.

### Use of fractional IPV doses (fIPV)

#### Current IPV supply situation

The two global IPV manufacturers, Bilthoven Biologicals and Sanofi Pasteur, have faced problems in their production processes and consequently made offers to the global market that fall short of meeting the global demand for IPV. Global IPV shortages are likely through at least 2018, with possible improvements foreseen by 2020.

Bilthoven Biologicals is the only manufacturer through the RF that offers IPV in vials (US\$1.90 per dose). The other IPV manufacturer offered a limited quantity of IPV doses in pre-filled syringes (US\$5.30 per dose), which has helped to reduce supply gaps but does not meet the Region's total demand.

As a result of efforts among countries, PAHO's Revolving Fund for Vaccine Procurement and the Comprehensive Family Unit (FGL/IM) have made adjustments to the vaccine delivery schedule. Thanks to maintaining opening lines of communications with manufacturers, countries have also received sufficient vaccine to complete polio vaccination schedules. However, even while maintaining these collaborative efforts, countries of the Region are estimated to begin facing IPV stock-outs as soon as July 2017.

#### Initial response to the limited IPV supply

In March 2016, based on available seroconversion data, SAGE recommended the use of two fIPV doses instead of one full IPV dose as an option to optimize available IPV supply at country level. In May 2016, TAG discussed the global IPV shortage and the supply situation in the Region in an ad-hoc virtual meeting. After reviewing evidence about the safety and immunogenicity of intradermal (ID) administration of two fIPV doses (0.1 ml or 1/5 of the complete dose), TAG recommended that countries reduce IPV wastage, prepare to respond to possible IPV shortages, strengthen outbreak response, evaluate the capacity for

the use of ID fIPV in the routine program, and strengthen epidemiological surveillance.

Since the last TAG recommendations on ID fIPV doses, the global supply situation has worsened. In March 2017, TAG held a subsequent ad-hoc virtual meeting to discuss the issue. At this meeting, TAG recommended that countries that administer more than 100,000 doses of IPV annually, and with the capacity to train healthcare workers and supervise ID fIPV implementation, should immediately begin preparing to implement a schedule of two fIPV doses followed by two or three doses of bOPV (Table 2). In the cases of Guatemala, Haiti, and the Dominican Republic, TAG recommended that these countries carefully evaluate their capacity to introduce a schedule with two fIPV doses, weighing the risk of stock-outs against training and supervision requirements and the need to achieve high coverage.

**Table 2. Regional recommendation for polio vaccination schedule, the Americas, 2017**

| Vaccination Schedule | Basic           |                 |                 | Booster         |                 |
|----------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                      | 1 <sup>st</sup> | 2 <sup>nd</sup> | 3 <sup>rd</sup> | 4 <sup>th</sup> | 5 <sup>th</sup> |
|                      | fIPV            | fIPV            | bOPV            | bOPV            | bOPV            |

#### Scientific evidence on the use of two doses of fIPV

The available scientific evidence shows that two doses of ID fIPV offer higher seroconversion for all polio serotypes than one full dose of IPV administered intramuscularly (IM). Additionally, studies show that the longer the interval between fractional doses, the better the immune response. Adverse events occur more frequently with ID than IM administration. However, these are generally mostly mild local reactions such as erythema and induration.

#### Programmatic and operational considerations of two doses of fIPV

Generally, ID administration of vaccines is generally more difficult than IM. Therefore, all healthcare workers should be adequately trained in safe vaccine administration. A timely supervision of ID fIPV implementation is needed to ensure the safety and effectiveness of the proposed change in strategy.

According to the WHO open-vial policy, IPV in multi-dose vials may be used for up to 28 days. For the application of fractional doses, a 0.1 mL

27G 3/8 syringe should be used, which is the same syringe used for BCG in some countries. However, some countries administer BCG in a 0.05 mL syringe and thus do not stock 0.1 mL syringes. According to information from the RF, most countries will likely not have 0.1 mL syringes available for BCG administration.

To introduce a fIPV schedule, updates to the registration system need to be taken into consideration during planning, training, and supervision. Additionally, the use of fIPV ID is based on scientific evidence but is not specified on the label, meaning that countries must follow the process of their respective National Regulatory Authority to use the vaccine off label.

TAG believes that as we get closer to the global polio eradication, several but all important recommendations will have to be considered:

### Recommendations

- Due to the global IPV shortage and evidence that a two-dose fIPV schedule provides better protection than one full IPV dose, TAG urges Member States to consider the implementation of two ID fIPV doses, followed by two or three bOPV doses, in lieu of one full IPV dose. Member States, with support from PAHO, should begin preparing training and communication activities with health workers on the application of ID fIPV.
- TAG reaffirms recommendations from May 2016, calling on Member States to reduce IPV wastage. In anticipation of possible IPV stock-outs, Member States should prepare for the operationalization of delivering bOPV in place of IPV until IPV becomes available, always maintaining at least four weeks between vaccine doses.
- TAG calls on the RF to continue to closely monitor the global supplies of IPV vaccine and 0.1 mL syringes, and to collaborate with vaccine manufacturers to reestablish a safe and affordable supply of IPV for the Americas.
- TAG endorses the regional polio risk assessment methodology and encourages Member States to conduct annual national polio outbreak risk assessments to determine risk at the district level. While some countries may have higher risks

POLIO continued from page 3

### Recommendations continued

than others, TAG stresses that all Member States in the Region remain at risk for polio importation until the disease is eradicated globally. Indeed, TAG expresses concern at the number of countries at high risk for poliovirus importation.

- TAG urges Member States that have not developed their national polio outbreak response plans (Bolivia, Brazil, Guatemala, Paraguay, and Uruguay) to do so and share these plans with PAHO.
- To maintain sufficient population-level immunity to keep the Region free of polio TAG urges Member States to ensure  $\geq 95\%$  coverage of three doses of polio vaccine nationally and in all municipalities.
- TAG reminds Member States of the need to ensure capacity to detect and respond to polio importations, especially calling on Member States to meet the minimum standards for AFP surveillance.
- TAG urges Member States to classify AFP cases as outlined in PAHO's Polio Field Guide (2006), categorizing cases based on lab results and follow-up evaluation. Compatible case should be considered failures of the surveillance system, and the NCCs and RCC should review such cases.
- TAG encourages each country to complete at least one containment report and commends Member States that have completed all four required elements of the containment reports.
- TAG encourages Member States to advance on the finalization of inventory of facilities with poliovirus infectious and potentially infectious materials, following the Containment Advisory Group guidance for completion of Phase I of GAP III.
- TAG encourages Member States with designated Polio Essential Facilities to officially nominate their National Authorities for Containment, and for Polio Essential Facilities to submit applications for the Certificate of Participation to their National. ■

## Mid-term Report on Achieving the Goals of the Regional Immunization Action Plan (RIAP)

In 2012, the World Health Assembly approved the Global Vaccine Action Plan (GVAP) 2010-2020. In the Region of Americas, the Regional Immunization Vision and Strategy (RIVS), 2010-2015, guided national immunization programs until the GVAP was adapted to the regional context and the Regional Immunization Action Plan (RIAP) took its place in 2016.

During the 2017 World Health Assembly, global health officials presented the GVAP Midterm Review, noting that adequate progress had been made in only one of the six targets set for this period. Unmet targets included reaching national and municipal coverage rate targets at  $\geq 90\%$  and  $\geq 80\%$ , respectively, in all countries; global polio eradication; maternal and neonatal tetanus elimination; measles elimination in at least five regions; and rubella elimination in at least two regions. The only target on track was the one set for new vaccine introduction. The GVAP Midterm Review suggested that slow progress may be related to low levels of country commitment or ownership; areas or populations with difficult access to vaccination services; weak epidemiological surveillance; mismanagement at different organizational levels; failure to ensure routine and timely data collection and analysis; a disconnect between the immunization program and health systems strengthening activities; social or armed conflicts; and outbreaks and other competing health emergencies and priorities.

In light of the concern regarding slow progress at global level, the World Health Assembly adopted *Resolution WHA70/A70.14*<sup>6</sup>, which urges WHO Member States to:

- Demonstrate stronger leadership and governance of national immunization programs
- Ensure the use of current, real-time data
- Strengthen surveillance
- View the program from the life course perspective
- Comply with recommendations of the International Health Regulations
- Mobilize domestic financing for vaccine purchases and program operations
- Strengthen international cooperation and domestic manufacturing to guarantee availability of affordable vaccines and technologies

According to the mandate of the PAHO's governing bodies, the Midterm Review (2015-2016) of the RIAP will be presented at the Pan

American Sanitary Conference in 2017. The Midterm Review describes the progress made to date, provides an in-depth evaluation of off-track targets, assesses the challenges and contextual factors that have delayed progress, and proposes solutions and actions that must be taken to achieve the targets by 2020.

The RIAP consists of four "Strategic Lines of Action": 1. Sustain the achievements; 2. Complete the unfinished agenda; 3. Tackle new challenges; and 4. Strengthen health services for effective vaccine administration. These four areas include seven General Objectives and six Strategic Objectives, and 29 indicators have been developed to monitor progress towards meeting the RIAP's objectives.

Since the inception of the Expanded Program on Immunization (EPI), PAHO and Member States have tracked vaccination coverage to monitor progress in immunization. The primary vaccination coverage indicator used to monitor program performance is the third dose of diphtheria-pertussis-tetanus containing vaccine (DTP3) in children aged  $< 1$  year. For much of the EPI's history in the Americas, DTP3 coverage increased steadily, reaching levels that were among the highest of all WHO Regions. In the last five years, in a sharp reversal of the historical regional trend, average coverage rates at the national and regional levels have plateaued and even dropped in some cases. In 2015, the average global DTP3 coverage had reached 87%, while regional DTP3 coverage dropped from 94% in 2011 to 91% in 2015.

To reduce risks associated with the reintroduction or the reemergence of eliminated or controlled vaccine-preventable diseases (VPDs), the RIAP set a goal for countries to reach  $\geq 95\%$  coverage of all vaccines at national and municipal levels. In 2015, 20 countries and territories reported national coverage  $\geq 95\%$ ; 13 reported coverage between 90-95%; six reported coverage between 80-90%; and four reported coverage  $< 80\%$ . Analysis at the sub-national level shows that 50% of municipalities in Latin America and the Caribbean (LAC) reported coverage  $< 95\%$  in the same year.

While achieving high and homogeneous coverage with the routine EPI immunization schedule is a challenge for the Region, countries and territories in the Americas continue to be leaders in introducing new vaccines, and in most cases, secure domestic resources to procure these vaccines. By 2016, 34 countries and territories had introduced pneumococcal conjugate vaccine (PCV) into their national immunization schedules, 20 had introduced

<sup>6</sup> [http://apps.who.int/gb/ebwha/pdf\\_files/WHA70/A70\\_R14-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R14-en.pdf)

RAIP continued from page 4

rotavirus (RV) vaccine, and 25 had introduced human papillomavirus (HPV) vaccine. This means that 90% and 85% of the regional birth cohort lives in countries where PCV or RV, respectively, is part of the routine schedule. Although HPV vaccine was introduced some years later, 80% of a typical adolescent girl cohort aged 9 years already has access to the vaccine through the routine program.

According to the Midterm Review presented to the Executive Committee of PAHO in June 2017, 16 of 29 monitoring indicators are on track, three are in progress, and 10 are off track.

The following indicators are on track:

- No cases of acute flaccid paralysis (AFP) due to poliovirus
- No reestablishment of endemic measles or rubella transmission
- Fulfillment of indicators to monitor quality of epidemiological surveillance for measles, rubella, and congenital rubella syndrome (CRS)
- Administration of Hepatitis B vaccine within 24 hours of birth
- Existence of national plans of action for immunization
- Monitoring of vaccine beneficiary satisfaction during Vaccination Week in the Americas
- Completion of cost-effectiveness studies before the introduction of new vaccines
- Completion of studies after introduction of new vaccines (impact assessments, operational reviews, etc.)
- Vaccination of pregnant women against influenza and/or tetanus-diphtheria
- Financing for immunization using domestic resources for  $\geq 90\%$  of total financing requirements

- Access to an adequate supply of quality vaccines
- Dropout rate  $< 5\%$  between the first and third doses of DTP
- Improvement in quality of coverage data
- Implementation of electronic immunization registries at the country level
- Post-marketing surveillance of vaccines
- Vaccination of health workers

Indicators considered to be in progress are:

- Neonatal tetanus incidence  $< 1/1,000$  registered live births
- Introduction of one or more new vaccines in the national schedule
- Integration of other preventive interventions with vaccination

Off-track indicators are:

- Indicators to monitor quality of epidemiological surveillance of AFP
- Existence of legal or administrative basis for immunization programs
- Existence of a National Immunization Technical Advisory Group (NITAG) meeting WHO criteria for good functionality
- National DTP3 coverage  $\geq 95\%$  in children aged  $< 1$  year
- DTP3 coverage  $\geq 80\%$  in each district or equivalent in children aged  $< 1$  year
- Monitoring vaccination equity through coverage analysis by income quintile
- Accuracy of supply and demand for vaccines procured through the Revolving Fund (RF)
- National DTP3 coverage  $\geq 95\%$  in children aged  $< 1$  year for three or more consecutive years

- Identification and correction of barriers to reaching unvaccinated or under-vaccinated populations
- Reporting of stock-outs of one or more vaccines or related supplies for more than one month at any level of the national structure

Based on the Midterm Review, the Executive Committee made the following recommendations to ensure adequate progress in achieving the goals of the RIAP:

- Improve legal frameworks
- Ensure that the benefits of immunization are equally shared by all
- Maintain and strengthen national commitments to immunization programs
- Strengthen disease surveillance
- Improve information systems
- Enhance communication and social mobilization

TAG noted that most unmet indicators involved the application of basic fundamentals of EPI strategies, such as coverage at the district level. While the EPI has ensured the control and elimination of VPDs in the Americas, governments need to recommit to the goals of the RIAP to sustain these significant achievements. The Midterm Review aims to increase awareness of challenges faced by the EPI in order to secure the necessary political commitment to address the crosscutting and program-specific vulnerabilities that put at risk decades of progress in the elimination and control of VPDs.

## Recommendations

- TAG commends Member States of the Americas for their continued commitment to the control and elimination of VPDs as demonstrated by the EPI's 40-year existence.
- TAG expresses serious concern about declining DTP3 coverage levels reported at regional, subnational, and national levels. TAG urges countries, with the support of PAHO, to locally assess and diagnose the underlying causes (societal perceptions, sociopolitical, economic, programmatic, etc.) of falling vaccination coverage targets, so that corrective actions can be designed and implemented.
- TAG endorses recommendations made in the Midterm Review of the RIAP to be presented at the PAHO Pan American Sanitary Conference in September 2017.
- Member States and the Pan American Sanitary Bureau should implement the recommendations issued in Resolution WHA70/A70.14 of the 2017 World Health Assembly, as well as the proposals of the Midterm Review of the RIAP.
- TAG urges PAHO and Member States to increase efforts to explain to policymakers and the public the importance of immunization and the considerable economic and health benefits arising from investments in strong national immunization programs. ■

## Meningococcal Vaccine Use in the Routine Immunization Program

Though its epidemiology varies substantially by capsular group, meningococcal disease (MD) is a global problem that affects all countries. Virulent strains of *Neisseria meningitidis* have a polysaccharide capsule, which is the major virulence factor of this bacterium. There are 13 diverse polysaccharide capsules, but only A, B, C, W, and Y commonly cause invasive infections. Information available on the epidemiology of meningococcal disease is incomplete, in part due to the absence of surveillance in many countries and inadequate bacterial detection methods. Due to the dynamic nature of the epidemiology of invasive meningococcal disease (IMD), the global distribution of the different serogroups of *N. meningitidis* may change over time.

The incidence of IMD is highest among infants aged <1 year and remains relatively high until children are about 5 years old. Although incidence tends to decrease among older children, it usually spikes during adolescence and young adulthood when individuals are living in close quarters. Incidence again tapers off in older adults.

While the current incidence of endemic MD in Latin American countries is typically <2 cases/100,000 population per year, epidemic disease has broken out in all parts of Latin American at different times in the past 40 years. The available data highlight the occurrence of MD epidemics in Latin American countries associated with different serogroups and reflect the unpredictable nature of the disease's epidemiology. The highest incidence rates were reported in Argentina, Brazil, Chile, and Uruguay, which are also countries with well-established surveillance systems. Brazil is the only country with information on age-specific incidence rates. In recent years, incidence rates have remained stable in LA countries, ranging between 1.5-1.8 cases per 100,000 inhabitants.

Between 2008-2010, the incidence in Argentina was 0.4-0.7 cases per 100,000 people. Among available isolates, 71% were serogroup B, 12% were serogroup C, and 10% were serogroup Y. In Uruguay, reported incidence rates ranged from 1.5-2 cases per 100,000 inhabitants. Venezuela reported incidence rates between 0.2-0.4 cases per 100,000 inhabitants during the last decade. In Cuba, from 1998 to 2003, the annual reported incidence of meningococcal meningitis among children aged 1-18 years ranged from 0.6-0.7 cases per 100,000 from 1998-2000 to 0.3 cases per 100,000 in 2003.

The case fatality rate (CFR) is high in Latin American, ranging from 10-20% in recent years

in several countries within LA, including Chile (14% in 2010), Argentina (7%-15%), Panama (12-15%), Mexico (18% in 2005-2008), and Uruguay (15%). In Brazil, during outbreaks before the introduction of the meningococcal C conjugate vaccine, CFR reached about 40% in those infected with this serogroup. Many survivors experience permanent debilitating sequelae, such as hearing loss, lost limbs, or neurological impairments.

Available meningococcal vaccines against serogroups A, C, W, and Y include both polysaccharide vaccines and polysaccharide-protein conjugate vaccines based on the meningococcal capsule. For serogroup B, vaccine development has included protein vaccines based on the meningococcal outer membrane vesicle (OMV), and the application of new genomic and proteomic approaches has led to the identification of a large number of novel protein vaccine antigens to prevent meningococcal disease.

**Polysaccharide vaccines:** Their use is now limited because they do not generate adequate immune response among children aged <2 years. Moreover, among patients aged >2 years, polysaccharide vaccines offer protection of limited duration and do not induce immune memory.

**Polysaccharide-protein conjugate vaccines:** Conjugate vaccines use a carrier protein to present polysaccharide antigen to the immune system, in a manner that induces a T-cell immune response. Although these vaccines have a good safety profile, questions remain regarding their long-term effectiveness and how to optimize vaccination programs.

To date in Latin America, four countries use a meningococcal vaccine in their routine immunization programs: Argentina (ACWY conjugate), Brazil (C conjugate), Chile (ACWY conjugate), and Cuba (B polysaccharide).

In Brazil, routine infant immunization with meningococcal C conjugate (MCC) vaccination started in November 2010, scheduled at age 3 and 5 months, plus a booster at age 12-15 months without catch-up. Recent studies have shown that the vaccination of infants and toddlers reduced meningococcal C invasive disease in the target population and the upcoming catch-up dose at age 12-13 years will accelerate the decrease in meningococcal C incidence rates among adolescents in Brazil.

Available vaccines tend to be costly. Given the high price of introducing this vaccine into routine immunization programs, countries considering its inclusion in the routine immunization schedule should consider the sustainability over time and ensure that other aspects of the immunization program such as training, supervision, and activities to increase vaccination coverage and epidemiological surveillance, are not affected by the vaccine's introduction.

The Revolving Fund should play a key role in negotiating vaccine prices with manufacturers, in order to reach a more affordable price for countries considering introduction of meningococcal vaccine into their routine programs. However, the lack of alternative manufacturers to stimulate competition is a major barrier to successful negotiations.

### Recommendations

- TAG urges Member States to expand from sentinel to nationwide surveillance of bacterial meningitis to better understand the epidemiology of the disease (including the age and serogroups distribution) and to detect outbreaks in a timely manner.
- In their decision-making on meningococcal vaccine introduction, TAG reminds Member States that they should review the disease's epidemiology, its burden and costs, the vaccine efficacy, safety, price, and duration of protection, and logistical and operational aspects of the immunization program.
- For a more accurate assessment of the vaccines' cost-effectiveness, TAG recommends that Member States include assessments of the long-term sequelae of meningococcal disease in these analyses.
- TAG reminds Member States that carriage studies contribute valuable information about disease transmission. However, these studies are not essential for decision-making on the use of a vaccine; they tend to be costly, complicated, and difficult to interpret.

## Plan of Action for Sustaining the Elimination of Measles and Rubella in the Americas

During PAHO's 55th Directing Council on 27 September 2016, the International Expert Committee (IEC) for Documenting and Verifying Measles and Rubella Elimination announced that after reviewing all of the epidemiological evidence presented by Member States for the period 2011-2016, the Region of the Americas had eliminated measles. The Region had reached the goal of eliminating endemic transmission of the measles virus in 2002 and had maintained this elimination for over a decade, despite constant importations of the virus from other regions in the world. It is worth noting that because the outbreak in Brazil lasted over a year, the last endemic case in the Americas has been redefined to have occurred in July 2015.

Currently, the six WHO regions have adopted the goal of eliminating measles by 2020 and two have committed to eliminating rubella by the same year. However, with the exception of the Americas, no other WHO region has met the targets for measles and rubella elimination in 2015. In this global context, PAHO issued an epidemiological alert on 4 May 2017 due to the increase in reported measles cases in Europe and other regions. From early January 2016 to 1 May 2017, 37 European countries reported 7,847 measles cases, with 34% of these reported in 2017. Romania (3,181 cases) and Italy (1,549 cases) reported most of the cases. This situation puts the sustainability of measles elimination in the Region of the Americas at risk.

TAG also noted that situations in Haiti and Venezuela are very concerning for sustaining measles and rubella elimination in the Americas. Accordingly, PAHO will support these countries in organizing follow-up campaigns and building preparedness and response capacities in the case of importations of measles and rubella cases from other regions. Another challenge for the sustainability of measles elimination relates to arbovirus outbreaks (e.g., Zika, Chikungunya, and dengue) in the Americas. Due to shared syndromic case definitions with measles, coordinated action and integrated analysis of febrile rash illness surveillance must be strengthened.

Finally, although MMR1 regional coverage has been 93-94% in recent years, there continue to be variations in coverage levels between and within countries at the municipal level. Accordingly, TAG has reaffirmed recommendations from other meetings, emphasizing the need to apply four criteria for quality—efficacy, efficiency, homogeneity, and opportunity, which PAHO is promoting by planning, executing, and evaluating follow-up vaccination campaigns. Likewise, it is important to remember that reducing the age of vaccination to 18 months (or to the

age at which the country applies the first DTP booster) for MMR2 implies that Member States must guarantee that at least ≥95% of children that have not received this dose in the routine program or during other follow-up campaigns are vaccinated.

PAHO/WHO is proposing a *Plan of Action for the Sustainability of Measles, Rubella and Congenital Rubella Syndrome Elimination in the Americas 2018-2023* at the next Pan American Sanitary Conference in September 2017. The plan aims to sustain a high level of immunity in the general population and to maintain high-quality surveillance systems to avoid the re-establishment of endemic transmission. The plan has four strategic lines of action with corresponding objectives and indicators:

**1) Guarantee universal access to measles and rubella vaccination services for the population targeted in the routine vaccination program and other at-risk age groups.**

Member States should implement activities to reach homogeneous coverage of ≥95% in all municipalities with two doses of MMR vaccine in children aged <5 years, through the regular vaccination program in health services and follow-up vaccination campaigns that have been planned and conducted using high-quality criteria.

**2) Strengthen the capacity of epidemiological surveillance systems for measles, rubella, and congenital rubella syndrome.**

Countries should implement activities to ensure fulfillment of surveillance indicators, which have suffered in the past two years, particularly with the low reporting of suspected measles and rubella cases in most countries.

**3) Develop national operational capacity to maintain measles and rubella elimination.**

The roles of the national commissions and regional commission should be maintained, with new terms of reference to monitor sustainability plans for measles and rubella elimination in future years.

**4) Establish standard mechanisms for rapid response to imported cases of measles, rubella, and CRS to prevent the reestablishment of endemic transmission.**

Creating, maintaining, or reactivating an immediate response group in each country is vital, with training in standard reporting,

research, and outbreak closure mechanisms for measles and rubella to ensure and verify the interruption of viral transmission. PAHO will make the necessary tools available to countries to improve response quality and time for measles and rubella outbreaks, starting with imported cases of viruses.

### Recommendations

- TAG urges Member States to prepare to implement the Plan of Action for the Sustainability of Measles and Rubella Elimination (2018-2023) following its adoption by the Pan American Sanitary Conference in September 2017.
- TAG emphasizes the importance of achieving and sustaining vaccination coverage ≥95% with two doses of measles and rubella vaccine.
- Member States should adhere to the previously recommended schedule that includes the second dose of the measles and rubella vaccine at the age of 18 months.
- TAG urges Member States to introduce the second dose of measles-containing vaccine (MCV), if they have not already done so. The two-dose series must be complemented by periodic follow-up vaccination campaigns as needed to close the immunity gaps.
- TAG emphasizes the need to strengthen the surveillance of fever and rash for measles and rubella and integrate it with that of dengue, Zika, Chikungunya viruses, and other illnesses that use the same syndromic definition, taking into account the epidemiology of such diseases in each country.
- Member States should continue building capacity for the early detection of imported cases and subsequent rapid response.
- TAG urges Member States to conduct risk assessments and identify susceptible populations that should be targeted with vaccination interventions, such as follow-up MR vaccination campaigns when indicated. These activities should minimize or mitigate the risk of importation and subsequent reestablishment of measles and rubella in the Region. ■

Starting in 2015, the Immunization Newsletter is being published four times a year, in English, Spanish and French by the Comprehensive Family Immunization Unit of the Pan American Health Organization (PAHO), Regional Office for the Americas of the World Health Organization (WHO). The purpose of the Immunization Newsletter is to facilitate the exchange of ideas and information concerning immunization programs in the Region, in order to promote greater knowledge of the problems faced and possible solutions to those problems.

An electronic compilation of the Newsletter, "Thirty years of Immunization Newsletter: the History of the EPI in the Americas," is now available at: [www.paho.org/inb](http://www.paho.org/inb).

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**Pan American  
Health  
Organization**



**World Health  
Organization**

REGIONAL OFFICE FOR THE **Americas**

## Letter from Dr. Fernando Muñoz, winner of the PAHO Immunization Award 2017, thanking PAHO Director Dr. Carissa Etienne

*We would like to share with our readers the letter Dr. Fernando Muñoz wrote to Dr. Carissa F. Etienne, Director of the Pan American Health Organization, thanking her for the PAHO Immunization Award, conferred at the XXIV Meeting of the TAG in Panama. Dr. Muñoz, who was unable to accept the award in person due to health issues, passed away on 12 October 2017.*

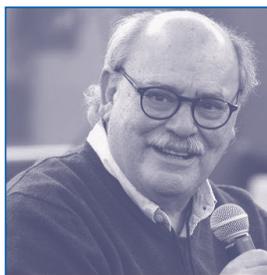
Santiago, 21 September 2017

It would have been a great pleasure to accept the PAHO Immunization Award in person, but my health has taken a turn for the worse and my treatment prevents me from doing so. Thus, I am expressing my gratitude from a distance to tell you how proud I am to be the recipient of this honor.

Vaccines have been closely tied to my professional and personal development since the start of my career and, in particular, with my appointment to the position of Pediatrician and Public Health Specialist on the faculty of a new medical school created by the University of Chile in Temuco, capital of the Region of Araucanía, an indigenous area that is the poorest region of Chile.

The year was 1978. A dictatorship had seized control of the country, and all of us who had embraced leftist ideas were suspect. Thus, coordinating my teaching responsibilities with the government Health Service was difficult. To give you an idea of just how problematic it was then to coordinate teaching activities with the authorities—who, in the wake of the military coup, warily supervised the survivors of one of the greatest persecutions of health workers ever—three physicians, including the director of Temuco Hospital, were among dozens of people abducted and killed in Araucanía by agents of the state, on top of the thousands of others who still represent an open wound in the fabric of Chilean society.

The person who saved me from cloistering myself in the classroom was noted public health expert Dr. José Manuel Borgoño, who had selected the Region to begin



**Fernando Muñoz.**  
Credit: PAHO/WHO.

implementing the training modules of the Expanded Program on Immunization (EPI) and needed someone with my profile to join a team of nurses and epidemiologists who would hold intensive workshops designed to significantly improve the coverage and quality of vaccination programs in the Region.

This was no easy task.

It was necessary to ensure proper cold chains from the manufacturer down to the child vaccinated in a health center or remote rural health post, which meant inspecting the refrigerators in health centers, cautioning that they were to be used exclusively for vaccines, providing them with minimum/maximum thermometers, guaranteeing protocols, and preparing manuals—all this, relying on the strength and commitment of our nursing teams.

Through these experiences, I have stayed connected with the immunization programs to this day. Over the years, I have been fortunate to have held positions that have enabled me to make important decisions about the Chilean program that have had a positive impact on people's health, especially children's health.

An experience that impacted me during my professional journey in immunization was getting to know the great Ciro de Quadros, who invited me to join the Technical Advisory Group (TAG) and assigned me a number of tasks aimed at increasing vaccination in the health services and fighting to make it institutional practice. This was fundamental, because while vaccination can be supplemented

with campaigns, its institutional anchoring is key to guaranteeing sustainable immunization programs.

My work in the TAG has been one of the most enriching experiences of my professional life. Working under D.A. Henderson, for example, was a privilege for which I have always been grateful and one that enabled me to experience up close the monumental efforts that he spearheaded to eradicate smallpox. The TAG has provided—and continues to provide—key guidance that explains much of the success in controlling vaccine-preventable diseases in the Region of the Americas.

This brings us to the present, a time of complexity and uncertainty. Our programs face growing challenges of a diverse nature. In this letter of thanks, I will limit myself to mentioning but a few of them:

- The need to guarantee sufficient primary care coverage to ensure that immunization of the entire population by government and certified private services is on sound footing.
- Transparency in relation to industry and the development of critical, evidence based capacities to counteract pressure from commercial interests.
- Studies on the attitudes of people and groups that oppose vaccines and, based on the knowledge gained, serious efforts to combat anti-vaccination propaganda.
- Placing more emphasis on the importance of immunization programs in the undergraduate training of health professionals, especially nurses.
- The need for steady expansion and improvement of immunization and vital statistics records to obtain reliable indicators that are comparable among countries.

My dear Dr. Etienne and PAHO colleagues, thank you again for this award. I hope to see you once this bitter cup that life has set before me is taken away. ■