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XX TAG Meeting Paving the Way for Immunization

The XX Meeting of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases of the Pan American Health Organization (PAHO) was held from 17-19 October 2012 in Washington, D.C.

The twentieth TAG Meeting addressed several topics including polio vaccines; use of thiomersal in vaccines; age restriction on rotavirus vaccine administration; Decade of Vaccines; evidence on pertussis; proposal for standardizing PAHO's TAG procedures; PAHO's Revolving Fund in the current global vaccine market; improving regional vaccine production capacity to meet the needs of the Americas; measles, rubella and Congenital Rubella Syndrome (CRS) elimination in the Region of the Americas; Haiti's immunization program; and cholera vaccination in the Americas.

The slogan for the meeting, "Paving the Way for Immunization," reflected the Region's leadership in immunization in the global context. The purpose of the meeting was to draft TAG recommendations on how to address current and future challenges facing immunization programs in the Americas. The following is a summary of TAG's technical deliberation and recommendations as presented in the final report. ■

Members of the Uru Chipaya Ethnic Group of the Oururu Department of Bolivia receiving the 2011 PAHO Immunization Award

In This Issue

Bolivian Uru Chipaya Community Receives PAHO Immunization Award

The Uru Chipaya Ethnic Group of the Oruro Department of Bolivia received the 2011 Pan American Health Organization (PAHO) Immunization Award for their activities to keep immunization coverage close to 100% in their area. The group was presented with a certificate of recognition, as well as a monetary gift in the amount of three thousand US dollars at the twentieth Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases. PAHO created the Immunization Award to recognize outstanding contributions to a national immunization program and to the control and/or elimination of vaccine-preventable diseases.

Despite extreme poverty conditions, marginalization and inequity, the Uru Chipaya Ethnic Group of Bolivia made extraordinary contributions in the control and elimination of vaccine-preventable diseases. In the last 15 years, the municipality reached more than 95% vaccination coverage, even reaching 100% coverage in some years. Since 2000, the community no longer has confirmed cases of measles, rubella or neonatal tetanus, in addition to other vaccine preventable diseases, such as polio and diphtheria, which have not occurred in 24 years.

Their achievements were made possible by making immunization and health promotion a top priority. In 2001, the community put nearly 60% of its financial resources into health, education and basic hygiene. The group established and maintained a strong alliance with the community, indigenous authorities and health personnel. Other activities to increase success in health included the development and use of creative tactics to prevent morbidity and mortality in the community; ensuring vaccination completion for teenagers, senior citizens and migrant groups; increasing vaccination hours; and promoting health in schools. ■

Polio Vaccines

At its most recent meeting held in Geneva on 10-12 April, the Strategic Advisory Group of Experts (SAGE) on Immunization recommended that, the World Health Organization (WHO) should promote switching from the trivalent oral polio vaccine (tOPV) to the bivalent oral polio vaccine (bOPV) for routine vaccination. This change should take place in a synchronized manner in order to minimize the risk of cVDPV2 circulation and outbreaks, as well as to accelerate the elimination of type 1 and type 3 wild viruses, since the bivalent vaccine provides better protection against those virus types than the trivalent vaccine[1].

During its 65th meeting in May 2012, the World Health Assembly (WHA) adopted Resolution WHA65.5, which states that "substantial planning is required for a globally synchronized switch from trivalent to bivalent oral poliovirus vaccine for routine immunization and, potentially, the introduction beforehand of one or more doses of inactivated poliovirus vaccine. In 2012, the SAGE will provide recommendations on the actual implementation of this strategy based on broad-based consultations across a number of work streams." In the Resolution, the WHA asks WHO's Director-General to undertake the development, scientific vetting, and rapid finalization of a comprehensive polio eradication "endgame" strategy, and inform Member States of the potential timing of a switch from trivalent to bivalent oral poliovirus vaccine for all routine immunization programs[2].

PAHO's TAG discussed the implications of a potential change in vaccination recommendations, noting that the Region of the Americas managed to eliminate wild poliovirus in 1991; and since then has remained free of polio without outbreaks due to importation, using the tOPV vaccine.

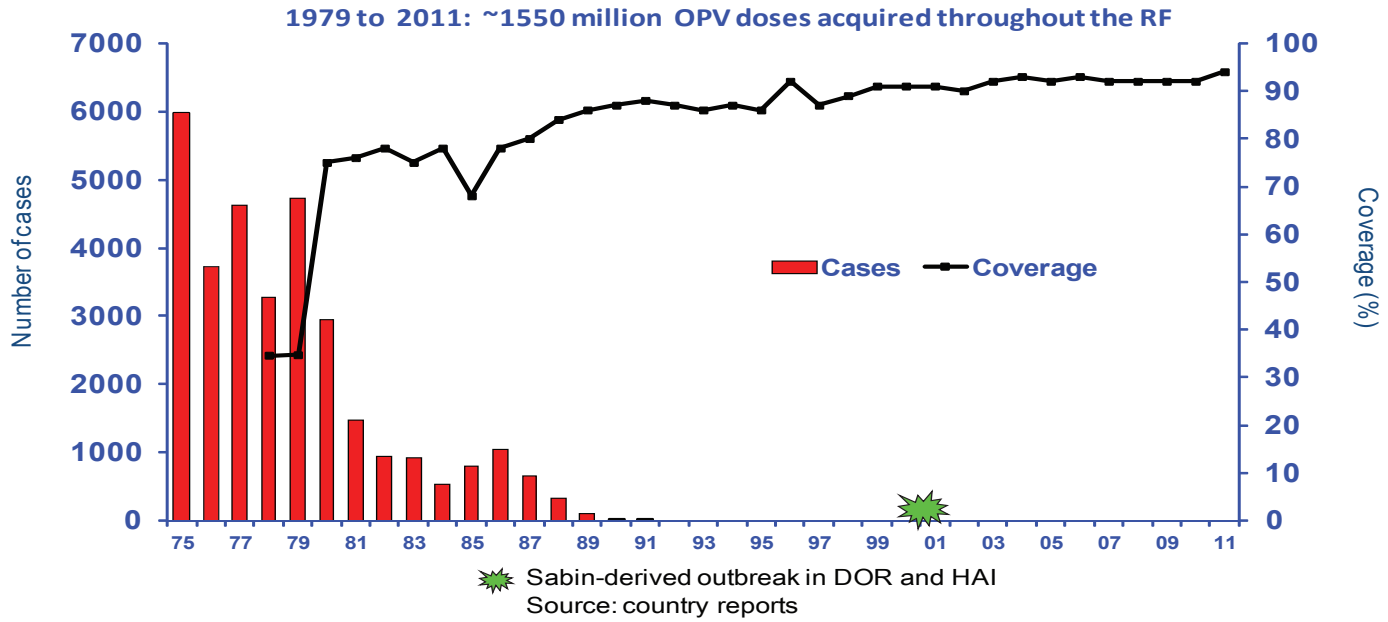
Recommendations:

- TAG awaits the World Health Organization's comprehensive polio eradication and endgame strategy, as well as results from ongoing and planned research to revisit its recommendations for the Region of the Americas. At the present time, the trivalent oral poliomyelitis vaccine (tOPV) remains the vaccine of choice for the Americas. To this end, PAHO, in collaboration with WHO, should negotiate with providers to ensure sufficient supply of tOPV for countries of the Americas.
- Countries considering the introduction of the inactivated polio vaccine (IPV) should first fulfill the sanitation and vaccination coverage conditions recommended during TAG's previous meeting (Argentina 2011). If a country does not meet these basic conditions, it should conduct at least two annual vaccination campaigns, administering the tOPV to every child aged <5 years, without taking into account their previous vaccination status. Countries making plans to introduce the IPV should be able to guarantee its long-term supply, in addition to considering the price of the vaccine.
- Countries should reinforce surveillance of AFP, attain adequate levels in all basic surveillance indicators, and continue working to achieve ≥95% polio coverage in every municipality.
- As IPV will be considered for use in the polio endgame requested by the WHA, it will be important for WHO to maintain a fluid dialogue with vaccine manufacturers to ensure an adequate IPV supply at an affordable price for countries of all income levels, as this will be a factor in the rapid adoption of the vaccine.
- PAHO is in an advantageous position to work with the GPEI, in the development of the endgame strategy and for the synchronized cessation of vaccines containing poliovirus type 2, and supporting cost-effectiveness studies for different scenarios. Additionally, the World Immunization Week could be used as an effective platform for globally coordinated actions. ■

1 Available at: http://www.who.int/wer/2012/wer8721.pdf

2 Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_R5-en.pdf

Polio3 coverage in children under 1 year of age and Polio cases in the Americas, 1975- 2011



Rotavirus Vaccination Schedule

Currently, the vaccination schedules used in Latin America and the Caribbean follow the most recent WHO position paper, which recommends administering the first dose of the vaccine between 6 and 15 weeks of age and the last dose no later than 32 weeks of age (2nd dose for the monovalent rotavirus vaccine and 3rd dose of the pentavalent rotavirus vaccine)[1].

More importantly, risk/benefit analysis continues to favor early immunization, but current age-related restrictions on administration of the first dose (<15 weeks) and the last dose (<32 weeks) prevent vaccinating many vulnerable children. If these restrictions were eliminated, children who are currently excluded from the benefits of rotavirus vaccines could be immunized, and it is likely that these include some of the children most vulnerable to this serious disease. Thousands of deaths could be averted, with just a minimal increase in cases of intestinal intussusception. SAGE also stated that based on the age distribution of rotavirus disease, vaccinating children over 24 months of age would have few beneficial effects.

1 Available at: http://www.who.int/wer/2009/wer8451_52.pdf

Recommendations:

- In the Region of the Americas, countries should continue making efforts to administer rotavirus vaccines on their routine immunization schedules, at the recommended ages, usually at 2 and 4 months or 2,4, and 6 months. This schedule favors the early immunization of children at greater risk of morbidity and mortality due to rotavirus diarrhea. However, in areas of difficult access and /or high diarrheal mortality, vaccine can be administered later, at any time of immunization contact and before 1 year of age.
- TAG encourages countries that have not introduced rotavirus vaccine to reassess the burden of disease in order to consider the introduction of rotavirus immunization. This in light of the current evidence demonstrating the huge impact of rotavirus vaccine administered in the current schedule in reducing the morbidity and mortality from rotavirus diarrhea in the Region of the Americas. ■

Measles, Rubella and CRS Elimination in the Region of the Americas

On 20 September 2012, ministers of health of the Region approved an emergency plan of action to keep the Americas free of measles, rubella, and congenital rubella syndrome (CRS) at the 28th Pan American Sanitary Conference. Given the continuing circulation of measles and rubella viruses in other regions of the world, countries of the Region continue to be exposed to high risk of virus importations. Moreover, some countries have reported weaknesses and failures in their national surveillance systems and routine immunization programs, making them vulnerable to the reintroduction of viruses that can cause outbreaks.

The emergency plan of action was formulated for the next two years to address weaknesses identified in the immunization and surveillance programs during the process to document and verify measles and rubella elimination. To sustain and build on this elimination achievement, PAHO has urged Member States to maintain high-quality, elimination-standard surveillance and high population immunization coverage against measles and rubella (>95%). Full implementation of intensified vaccination activities to maintain elimination status will be essential to ensure high immunization coverage, especially in areas that have susceptible populations. As part of the emergency action plan, countries should integrate the proposed activities for maintaining measles, rubella, and CRS elimination in their annual plans of action for national immunization programs.

Recommendation:

The TAG endorses and urges countries to implement the Emergency Plan of Action to maintain the elimination of measles, rubella and CRS in the Americas, as stated in Resolution CSP28.R14 of the Pan American Sanitary Conference 2012. ■

Evidence on Pertussis

Pertussis continues to be a significant cause of child mortality worldwide and a disease that causes serious public health concern, even in countries with high levels of vaccination coverage. The WHO estimates that in 2008, there were nearly 16 million cases worldwide, 195,000 of which resulted in death.

In the Region of the Americas, coverage with DPT3 among children aged <1 year is over 90%, and the annual number of cases has ranged from 15,000 to 34,000 over the last 10 years, with significant increases in the number of cases in Argentina, Brazil, Chile, Colombia and the United States in the last year.

During its last two meetings, the TAG discussed matters related to this disease and issued recommendations. It also clearly stated that in order to change or issue new recommendations, it requires new epidemiological information to support them. In response to this call for action, a project titled "Improving Epidemiological Surveillance of Pertussis in Latin America" is now being carried out in Argentina, Mexico and Panama, with support from the Sabin Vaccine Institute, the US Centers for Disease Control and Prevention (CDC) in Atlanta, the and PAHO. Its objectives include: improving diagnostic capacity, developing a reliable and valid method of improving surveillance of pertussis in Latin America, and making the project findings and results available by the end of 2012.

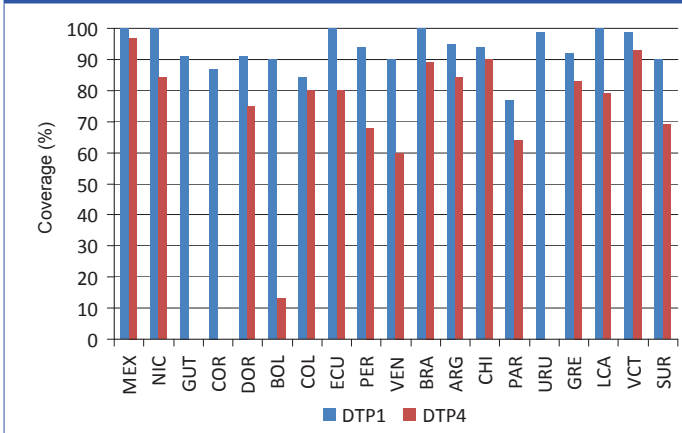
In March 2012, 32 professionals from 12 countries in the Region participated in a meeting called by PAHO to define what information is needed or could be presented to request that the TAG issue new recommendations or to implement the current recommendations. The countries were invited to present new epidemiological evidence. The conclusion drawn from the meeting was that the disease continues to appear among children under five without completed vaccination schedules for their age. No additional new evidence was presented to support new recommendations. The goal continues to be adequate implementation of the current recommendations.

During this meeting, the TAG received an update on the global pertussis situation, new trends in vaccination policies such as the "co-

coon" strategy and vaccination of pregnant women, and a report on the current status of the "Improving Epidemiological Surveillance of Pertussis in Latin America" project. Argentina, Chile, Mexico, and the United States presented information on recent pertussis outbreaks and the measures taken for their control. It was highlighted that a significant proportion of cases and deaths occur among infants, often in the first months of life.

There is growing evidence of an increase in the incidence of the disease in adolescents in some settings, which suggests that the immunity conferred by the acellular vaccine is short-lived. In September 2012, WHO convened an informal expert meeting to discuss the current situation of pertussis in Australia, Canada, the United Kingdom, and the United States. The experts concluded that there are limitations to aP, but that the problem remains poorly defined. At that meeting, it also was highlighted that countries are utilizing a range of strategies, including maternal vaccination and cocooning; and that use of aP or the Tdap booster is being contemplated. However, the data available to support these strategies is weak. Similarly, at this time there is insufficient evidence to support the use of a 5th DTP dose. It is expected that SAGE will review pertussis vaccination strategies in use at upcoming meetings.

Reported DTP1 and DTP4 Coverage, Selected Countries of the Americas, 2011



Only includes countries reporting DTP4 coverage in the 2012 PAHO/WHO-UNICEF Join Reporting Form on Immunization

Recommendations:

- Countries should ensure vaccination coverage ≥95% with 3 doses of pertussis-containing vaccines in children aged <1 year; and encourage timely vaccination and completion of the schedule. The 4th dose of the DPT vaccine should be incorporated into the regular vaccination program in every country, and the coverage attained with this dose (as with all vaccine doses) should be the object of careful recording, monitoring, reporting and evaluation.
- Every pertussis outbreak should be thoroughly investigated to improve the understanding of the current epidemiology of the disease in the Region of the Americas. PAHO should provide countries with specific guidance for outbreak investigation.
- Countries should improve surveillance and the use of adequate diagnostic tools. The present surveillance pilot project being implemented in Argentina, Mexico and Panama by the Sabin Vaccine Institute, CDC and PAHO should be expanded to other countries of the Region.
- Considering new evidence suggesting that the immunity conferred by the acellular vaccine may be shorter-lived than the immunity conferred by wP vaccines, countries that are using whole-cell vaccine (wP) should not switch to an acellular vaccine (aP). Similarly, countries currently using aP should not switch back to the use of wP until more evidence is available to support changes in vaccination strategies for pertussis. ■

Decade of Vaccines: From Planning to Action

The Global Vaccine Action Plan (GVAP) is the result of global consultation efforts, which gathered input from more than 1,100 people from 142 countries and 297 organizations in Asia, Africa, the Americas, Europe, the Middle East and the Western Pacific. The GVAP builds on the success of the WHO/UNICEF 2006-2015 Global Immunization Vision and Strategy (GIVS), which was launched in 2005 as the first 10 year strategic framework for immunization. The plan reiterates existing goals and sets new goals for the Decade of Vaccines (DoV) 2010-2020, proposes six strategic objectives and provides an initial estimate of resource requirements and return on investments.

On May 25, 2012, the 65th World Health Assembly (WHA) endorsed the GVAP and passed resolution 65.17 in support of it. Beyond the action plan, country, regional and global stakeholders need to take responsibility for specific actions, translate the action plan into detailed operational plans, complete the development of the monitoring and accountability framework for the DoV, and mobilize resources to ensure the vision for the DoV becomes a reality.

In the Americas, the GVAP will complement the existing Regional Immunization Vision and Strategy (RIVS), which was developed to translate the GIVS into regional priorities in the late 2000s. The RIVS has three strategic areas to guide the implementation of successful immunization programs in Latin America and the Caribbean, including strategies for: maintaining the achievements; completing the unfinished immunization agenda, with the control of vaccine-preventable diseases; and facing new challenges, such as the introduction of new vaccines. Likewise, the GVAP encompasses these same strategies but with a more horizontal approach, highlighted in its six strategic objectives (SOs):

(SO1): All countries commit to immunization as a priority

(SO2): Individuals and communities understand the value of vaccines and demand

(SO3): The benefits of immunization are equitably extended to all people

(**SO4**): Strong immunization systems are an integral part of a well-functioning health system

(SO5): Immunization programs provide sustainable access to predictable funding, quality supply and innovative technologies

(SO6): Country, regional and global research and development innovations maximize the benefits of immunization

The six strategic objectives set forth in the GVAP will help bring new focus to the existing RIVS. PAHO's regional immunization program will work to incorporate the six strategic objectives described in the GVAP into its existing RIVS framework by developing a regional vaccination action plan to 2020 and beyond. For this regional action plan, PAHO will lead discussions with Member States to develop and define indicators to track progress towards achieving regional goals and targets. ■

Cholera Vaccination in the Americas

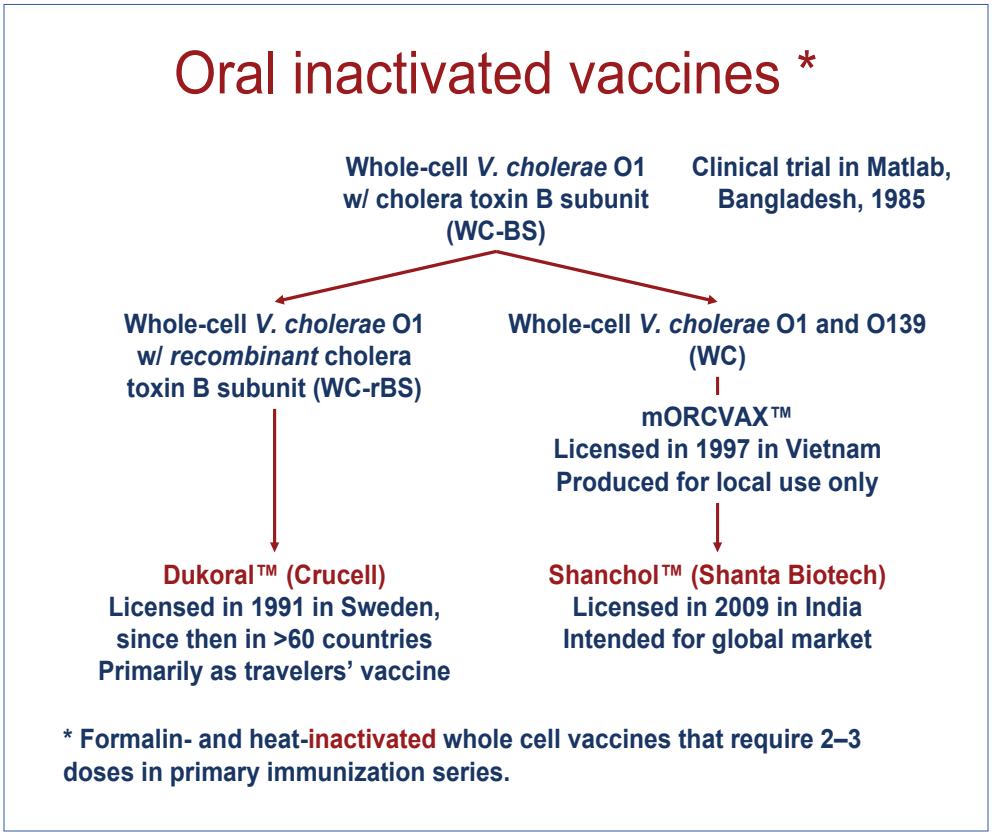
Deployment of oral cholera vaccine (OCV) has been considered since October 2010. At that time, also considering the rapidly spreading epidemic and the limited vaccine supplies, PAHO recommended focusing emergency efforts on time-tested measures for cholera outbreak response, namely on treatment to prevent deaths and traditional preventative actions to halt transmission (i.e. delivery of safe potable water, provision of supplies for hand washing and other hygienic measures, sanitation, and proper waste disposal). An expert consultation convened by PAHO in December 2010 recommended that the limited vaccine supply be used for demonstration projects and that efforts be initiated to increase OCV availability.

At least four elements warrant a reconsideration of OCV deployment in the Island of Hispaniola: the ongoing occurrence of cholera now almost two years after the epidemic began; the WHO-prequalification in September 2011 of a second OCV (Shanchol) that eases some operational challenges; the immediate availability in principle of up to 600,000 OCV doses; and the demonstration that, with substantial planning and logistic resources, OCV deployment is feasible on the Island1.

Most important, interventions to decrease cholera transmission through improvements in water and sanitation, as well as the provision of clean water and sanitation to every household will take years to accomplish and will require the mobilization of billions of dollars, while immunization against cholera offers immediate short-term benefits to support the long-term vision.

Recommendations:

- TAG commends the work of PAHO and partners for establishing and recently expanding the Regional Coalition on Water and Sanitation for the Elimination of Cholera in the Island of Hispaniola.
- Advocated by this Coalition, the elimination of cholera transmission in the Island of Hispaniola, defined as cholera no longer being a public health burden, will only be achieved in the long run through considerable investments towards significant and sustained improvements in access to potable water and sanitation. To achieve the overarching goal of cholera transmission elimination, TAG considers that several short-term actions should also be considered, including the expanded use of OCV. However, if water and sanitation are not improved in the long run, the Island will likely remain vulnerable to repeated epidemics, even with a large-scale cholera vaccination program in place.
- TAG recommends that OCV be used in Haiti, leveraging its delivery to strengthen the provision of other cholera prevention measures (i.e., social mobilization and active case-finding) and national immunization services. To reach this objective, incremental advances are needed in the integration of OCV use with Water, Sanitation, and Hygiene (WASH) development plans, in assuring sufficient OCV availability and financial sustainability of its purchase and delivery, and in developing operational and monitoring immunization capacities. These advances need to build national and local capacity of immunization programs and the health system as a whole. The timeframe during which vaccination will be needed depends on the advances in access to potable water and provision of sanitation and on the evolution of natural and vaccine immunities at population level. Contingent on firm orders, global production capacity could be scaled up to 2–4 million doses in 2013 and to 10–20 million doses in 2014 and thereafter. Therefore, a phased introduction based on global supply will need to be used in Haiti. OCV deployment could be prioritized in the following areas:
- a) OCV introduction as part of the routine national schedule for children aged one year linked to the delivery of the MR vaccine, b) in the metropolitan area, supplemental immunization activities (SIA) targeting internally displaced people residing in camps (i.e., a group with low immunity likely transitioning to higher risk circumstances) and/or larger populations residing in shanty towns (a group with current moderate to high immunity, but ongoing high risk circumstances), and c) in rural areas, through SIA targeting the population who have difficult access to health care. Vaccination in rural areas will most likely require additional prioritization based on geospatial analyses of a defined set of criteria defined a priori. Regardless of the time and eventual scope of a cholera vaccination program, additional resources and funds will be needed for the program to be successful, and without ongoing attention to strengthening water, sanitation, and hygiene, OCV use will not prevent long-term risk of disease outbreaks and resurgence. ■



1 Immunization Newsletter, February 2011, Vol. XXXIII, No. 1: Cholera Outbreak in Haiti. Available at: http://paho.org/inb/.

Thimerosal-Containing Vaccines Continue to be Safe

At its twentieth meeting held in October 2012, the Technical Advisory Group (TAG) on Vaccine-preventable Diseases recommended continuing the use of ethylmercury (thimerosal)-containing vaccines, following current vaccination schedules for children. In this way, the TAG revisits the recommendation of the Strategic Advisory Group of Experts on Immunization (SAGE) of the World Health Organization (WHO), which recognized that thimerosal-containing vaccines are safe and that replacing this compound with an alternative preservative could affect the quality, safety and effectiveness of vaccines.

The SAGE also established that the information available justifies the recommendation not to change WHO policy on immunization with respect to thimerosal-containing vaccines. Other expert groups (the Institute of Medicine of the United States, the American Academy of Pediatrics, the United Kingdom's Committee on Safety of Medicines, and the European Agency for the Evaluation of Medicinal Products) have reached similar conclusions.

For over 10 years, through its Global Advisory Committee on Vaccine Safety (GACVS), WHO has closely followed scientific evidence pertaining to the use of thimerosal as a vaccine preservative. Following the examination of available epidemiological information and the pharmacokinetic profile of this compound, it concluded that there was no evidence of mercury toxicity in infants, children or adults exposed to thiomersal from vaccines. Therefore, there is no safety-related reason to change current vaccination practices involving vaccines containing this preservative.

In response to the United Nations Environment Program's (UNEP) proposal to approve a world treaty to prohibit the use of mercury in every product or process, which would entail 1) replacing thiomersal in vaccines or 2) producing vaccines in single-dose vials without preservatives. In response to these two proposals, SAGE and TAG members reaffirmed that thimerosal-containing vaccines are safe and irreplaceable components of immunization programs, especially in developing countries, based on the following arguments:

1. The substitution of the preservative. The available alternative preservatives currently interact unpredictably with existing vaccines and there is no consensus for the use of these preservatives in the medium or long-term. Likewise, it would need to meet all the requirements of the regulatory authorities for its substitution. This could require a new license request, including performing new pre-clinical and clinical studies. This process is slow and expensive and could lead to an increase in the cost of the vaccine and even disrupt the global supply of vaccines. Furthermore, WHO does not currently have a program to evaluate alternative preservatives to thimerosal, given the lack of scientific evidence to suggest that its replacement is required.
2. The replacement of vaccines from multi-dose to single-dose vials: Currently, there is not enough capacity for the production of single-dose vials for the more than 325 million doses that are produced today; it would have important implications on the cold chain, storage, and final disposal and as a result, increasing the operational costs of immunization programs.

According to an analysis conducted by the Pan American Health Organization's (PAHO) Revolving Fund on the impact of removing thimerosal from vaccines, the cost of purchasing vaccines in the Americas would increase from $97 million to $770 million (7.9 times more). Furthermore, it would require more resources to guarantee adequate storage and transport of vaccines. A single-dose vial (1 dose) occupies, in terms of space, 19.2 cm^3/dose while a multi-dose vial (10 doses) occupies 4.4cm^3/dose. Lastly, the volume of annual vial waste would increase 4.2 times more, from 18.6 million vials to 70.3 million.

As a result, either of the two alternatives could endanger the success of the routine immunization programs as well as the vaccination campaigns with a predictable and significant increase in both morbidity and mortality along with very limited benefits for the environment. Finally, both the SAGE and TAG encouraged continuing the ongoing dialogue between the health and environmental sectors in the country in order to facilitate a common understanding of the important role of thimerosal-containing vaccines in the health of the population.

On Thimerosal and Vaccines

Mercury exists in different forms and compounds that can be found in the environment. Major sources of exposure include an accumulation of methylmercury within the food chain and through fish consumption. Meth-

Absence of Scientific Evidence on Harm—Conclusions of the GACVS

In 2000, WHO asked the Global Advisory Committee on Vaccine Safety (GACVS) to investigate safety concerns related to the use of thimerosal. From 2002 to 2008, the members of the GACVS reviewed several pharmacokinetic and epidemiological studies on thimerosal. According to the results of the pharmacokinetic studies conducted in children, including premature and low birthweight babies, the half-life of ethylmercury was 3-5 days; ethylmercury is excreted efficiently in the stool; and there is no long-term accumulation in the blood or tissues, as ethylmercury levels returned to average values less than 30 days after vaccination [4].

At its most recent meeting, the members of the GACVS examined the results of 28 published studies (from 2008 to the present) that measured short- and long-term blood mercury levels following vaccination, and epidemiological studies that examined the relationship between thimerosal and different health problems. Three ecological studies that suggested a causal relationship between neurodevelopmental disorders and thimerosal were discounted due to methodological errors. In addition, the steady increase in the number of autism cases diagnosed in the United States, despite the elimination of thimerosal from most vaccines administered in the country, was a convincing argument against any causal relationship. In the other epidemiological studies reviewed, which were conducted in different countries, no association with neurodevelopmental disorders could be identified.

As a result, GACVS concludes that the evidence available to date firmly supports the use of thimerosal as a preservative in inactivated vaccines. Research to gather new evidence of a causal relationship with thimerosal for scientific consideration should be conducted using the highest standards for causal inference in epidemiological studies. Thimerosal gives millions of people around the world access to safe vaccines, and to date, there is no safe and effective alternative.

ylmercury is a neurotoxic of major public health concern, with a half-life of approximately 50 days. Thiomersal, which is also known as thimerosal, mercuriothiolate and sodium 2-ethylmercuriothio-benzoate, is a compound that contains **ethylmercury**, and not methylmercury. It is used to prevent the proliferation of bacteria and fungus during storage and, above all, during the use of open multi-dose vials of certain vaccines. **Ethylmercury** has a very short life with a half-life of roughly a week; it is quickly excreted, and therefore does not accumulate in the human body.

Some vaccines may contain trace amounts of thimerosal even if it is not part of the final formulation of the product, because it may have been used in the production chain. This is true of inactivated vaccines to which this compound is added to maintain sterility during production. Thimerosal has been used since the 1930s in the manufacture of some vaccines and other medical products, and not only in pentavalent vaccines (DPT-Hib-HB).

Currently, thimerosal-containing vaccines are used in more than 120 countries to immunize at least 64% of the annual world birth cohort. These vaccines protect against four leading causes of death: diphtheria, tetanus, whooping cough, and *Haemophilus influenzae* type b. They have also been used in both the industrialized and developing countries to protect their populations against pandemic influenza [3].

The Source of the Concern

Since 1999, concerns have been raised about the possibility of adverse effects, autism in particular, following the use of thimerosal-containing vaccines. That year, the U.S. Food and Drug Administration (FDA) said that children who were vaccinated according to the immunization schedule for their age could be exposed to 187.5 µg of mercury, an amount that would exceed allowable methylmercury exposure levels.

As stated previously, thimerosal consists of **ethylmercury**, which is very different from the neurotoxic methylmercury. It is the methylmercury, not the ethylmercury, that causes histopathological brain lesions, and these are different from the ones found in autistic children.

It is important to clarify that the measles, mumps, and rubella (MMR) vaccine does not contain thimerosal.

Recommendations:

- Continue using ethylmercury (thiomersal)-containing vaccines, following current vaccination schedules for children.
- PAHO should mount an aggressive strategy and plan to effectively communicate and educate health care workers, as well as ministries of health and environment, parliamentarians, and other decision-makers, and the media on the safety of thiomersal-containing vaccines. ■

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The PAHO Revolving Fund and the Current Global Vaccine Market

For over three decades, as part of the Regional Expanded Program on Immunization (EPI) established in 1977, PAHO has managed the Revolving Fund (RF) for the procurement of vaccines and vaccination supplies on behalf of Member States.

Although the RF has gained relevant strengths and made significant contributions, it also faces considerable challenges including an insufficient supply of vaccines such as yellow fever vaccine, a reduction of the global supply of trivalent oral polio vaccine, a limited supply base of one or two laboratories for new vaccines and the existence of other stakeholders whose plans have an impact on the world vaccine market, specifically dose availability and prices of some vaccines for the Region.

The RF continuously seeks to address these challenges, while preserving its principles of Pan-Americanism, equity, universal access and quality.

Other important international actors related to vaccine procurement include UNICEF, GAVI Alliance, Bill and Melinda Gates Foundation (BMGF) and Doctors without Borders (Médecins Sans Frontières or MSF). These organizations were convened to the TAG meeting, highlighting the importance of having all of the key stakeholders involved in vaccine procurement and deployment strategies at the table for this discussion.

Recommendations:

- TAG congratulates PAHO's EPI Revolving Fund for vaccine procurement and reaffirms its support to the Fund as a key pillar of immunization programs in the Americas.
- TAG recommends that Member States continue to participate in the Revolving Fund to continue obtaining the benefits of a strong economy of scale in the procurement of vaccines, syringes and supplies.
- The Revolving Fund should continue improving vaccine forecasting, including newly available vaccines.
- PAHO should maintain its commitment to strengthen operating and financial management of the Fund in order to provide increasingly better service and greater credit capacity to participating countries and territories.
- In light of current challenges, PAHO should continue building its knowledge of global markets and strive for continuous communication and coordination with its major partners in the global immunization field, to maintain updated information on the markets where it participates, for the development of its procurement strategies.
- TAG recommends that all those agencies that deal with vaccine forecasting, procurement and distribution meet periodically to exchange information on their activities and strategies to identify those areas in which closer collaboration could facilitate the availability of vaccines, enhance security of supply, and encourage high quality at affordable prices. ■

The *Immunization Newsletter* is published every two months, in English, Spanish, and French by the Comprehensive Family Immunization Project 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.

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Comprehensive Family Immunization Project

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Improving Regional Vaccine Production Capacity to Meet the Needs of the Americas

The Region of the Americas has proven experience in vaccine development and production. Also, in LAC there are national regulatory authorities (NRAs) with improved capacity for monitoring vaccine quality, safety and effectiveness during the pre and post-marketing phases.

Vaccine production in the public, as well as the private field, has served to meet a significant portion of the demand from NIPs. Despite this fact, installed capacity has not necessarily been sufficient to cover growing regional demand, since in many cases the production volume is only geared toward fulfilling domestic needs, with little possibility of exporting vaccines. The establishment of technology transfer agreements between the transnational pharmaceutical industry and regional producers has not yet led to improvements in local capacity to produce new vaccines; therefore, a more thorough analysis of the role regional producers can play in meeting the needs of countries in the Region for safe, effective and high quality vaccines is needed.

Recommendation:

PAHO should convene a task group with representatives from vaccine manufactures from Latin America and the Caribbean (LAC) to identify common areas of work and brainstorm a LAC regional strategy for vaccine research, development and production. PAHO should then report back to TAG on this topic. ■

WANTED:

Members of Trinidad and Tobago's East Leo Club that collected money for PAHO's Revolving Fund for vaccine procurement in 1982

In 1982, Trinidad and Tobago's East Leo Club, formed of sons and daughters of Lions' Club members, collected money to contribute to capitalizing the Pan American Health Organization's (PAHO) Revolving Fund for vaccine procurement. Through a variety of initiatives, which included car washes and other community activities, the children's club collected $1,500 for the Fund.

Now that 30 years have passed and the RF manages a capital fund of $100 million and a purchase value of approximately $500 million, and buys about 60 different products for its participating countries, PAHO is looking for those people, then entrepreneur children, to better document that interesting experience. If you know any of these people, or were one of those children, we urge you to contact PAHO's immunization program at fch-im@paho.org

Reference

1. EPI Newsletter, February 1982, Vol. IV, No. 1: Donations to EPI Revolving Fund. Available at: http://paho.org/inb/.