Monitoring Measles Eradication in the Region of the Americas: Critical Activities and Tools

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The purpose of this paper is to discuss methods recommended and used by the Pan American Health Organization (PAHO) to monitor the interruption of indigenous measles transmission in the Region of the Americas. The methods used include house-to-house monitoring of vaccination coverage as a supervisory tool during both campaigns and routine vaccination; thoroughly investigating all measles outbreaks; performing routine surveillance, including weekly reporting from at least 80% of reporting units; and validating routine surveillance through active-case searches at health care institutions and schools and in the community. The strategies described have helped PAHO to increase the authority and accountability of vaccine program managers at the local, provincial, and national levels. Their efforts have permitted the Region of the Americas to reduce to three the number of countries with indigenous measles transmission and to reach a record low of 503 measles cases in 2001.

In 1994, the countries of the Americas set a goal of measles eradication [1–3]. During 2001 in the Region of the Americas, only 503 confirmed cases were identified, the lowest total ever and a 71% decline over the 1754 cases reported during 2000. Only three countries, Haiti and Dominican Republic (on the island of Hispaniola) and Venezuela (after a 2001 importation from Europe), had evidence of indigenous measles transmission during 2001 (table 1).

For the Region to reach and maintain the interruption of indigenous measles transmission in the absence of global eradication, it is crucial that vaccine program managers provide adequate supervision to the staff at the local level, routinely verifying the quality of the vaccination and surveillance efforts.

This paper discusses methods recommended by the Pan American Health Organization (PAHO) for monitoring vaccination coverage during regular visits of health centers by supervisors and during vaccination campaigns, for investigating measles outbreaks, and for performing and validating routine surveillance. It is not intended to discuss the pros and cons of any survey methodology or the guidelines being developed by PAHO for the use of sequential sampling. These will be the subject of a future PAHO publication.

**MONITORING VACCINE COVERAGE**

Official country reports are the main source of information on vaccination coverage. However, the population denominators used are often extrapolated from census data that are >10 years old, and population growth and rural-urban migration patterns have substantially changed since then, making census information often unsuitable for providing appropriate denominators for local vaccine program managers to determine vaccination coverage. The problem is often evident even with aggregated provincial or national data.
Table 1. Outbreak characteristics in 2000 and 2001 among countries that reported confirmed measles cases.

<table>
<thead>
<tr>
<th>Year, country</th>
<th>Suspected cases already discarded</th>
<th>No. of discarded cases/100,000</th>
<th>Total no. of confirmed cases</th>
<th>No. of sporadic cases</th>
<th>No. of outbreaks</th>
<th>No. of cases per outbreak</th>
<th>No. (%) of outbreaks linked to importations</th>
<th>Genetic characteristics and source of outbreak viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argentina</td>
<td>929</td>
<td>2.5</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>Unknown</td>
</tr>
<tr>
<td>Bolivia*</td>
<td>1391</td>
<td>16.7</td>
<td>122</td>
<td>3</td>
<td>66, 12, 11</td>
<td>0</td>
<td>D6 (endemic)</td>
<td></td>
</tr>
<tr>
<td>Brazil**</td>
<td>54,357</td>
<td>31.5</td>
<td>36</td>
<td>22</td>
<td>1</td>
<td>15</td>
<td>—</td>
<td>D6 (?) (endemic)</td>
</tr>
<tr>
<td>Canada*</td>
<td>6000</td>
<td>19</td>
<td>199</td>
<td>0</td>
<td>4</td>
<td>2, 6, 30, 165</td>
<td>4 (100)</td>
<td>D6, D7 (imported)</td>
</tr>
<tr>
<td>Colombia</td>
<td>2047</td>
<td>4.8</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dominican Republic*</td>
<td>3397</td>
<td>40</td>
<td>254</td>
<td>0</td>
<td>1</td>
<td>254</td>
<td>0</td>
<td>D6 (endemic)</td>
</tr>
<tr>
<td>Haiti***</td>
<td>187</td>
<td>2.3</td>
<td>990</td>
<td>0</td>
<td>1</td>
<td>990</td>
<td>0</td>
<td>D6 (endemic)</td>
</tr>
<tr>
<td>Mexico</td>
<td>2231</td>
<td>22.2</td>
<td>30</td>
<td>7</td>
<td>8</td>
<td>2–5</td>
<td>?</td>
<td>Imported (?)</td>
</tr>
<tr>
<td>Peru</td>
<td>5680</td>
<td>21.8</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>United States</td>
<td>1386</td>
<td>0.46</td>
<td>86</td>
<td>11</td>
<td>10</td>
<td>3–9</td>
<td>5 (50)</td>
<td>Imported (D6, D4, G2, D3)</td>
</tr>
<tr>
<td>Venezuela</td>
<td>1562</td>
<td>6.3</td>
<td>22</td>
<td>0</td>
<td>1</td>
<td>22</td>
<td>Unknown</td>
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<td>2001</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>38,679</td>
<td>18.2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>1 (100)</td>
<td>D4 (to be confirmed)</td>
</tr>
<tr>
<td>Canada</td>
<td>NA</td>
<td>NA</td>
<td>33</td>
<td>11</td>
<td>6</td>
<td>7, 3, 3, 3, 3, 3, 3, 6</td>
<td>6 (100)</td>
<td>H1, D3, D5 (imported)</td>
</tr>
<tr>
<td>Colombia</td>
<td>1514</td>
<td>3.5</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ecuador</td>
<td>1575</td>
<td>12.3</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>Unknown</td>
</tr>
<tr>
<td>El Salvador</td>
<td>372</td>
<td>5.9</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1 (100)</td>
<td>D7 (imported)</td>
</tr>
<tr>
<td>Mexico</td>
<td>717</td>
<td>0.7</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1 (100)</td>
<td>Unknown (imported?)</td>
</tr>
<tr>
<td>Dominican Republic*</td>
<td>1056</td>
<td>12.4</td>
<td>113</td>
<td>0</td>
<td>1</td>
<td>1132</td>
<td>—</td>
<td>D6 (endemic)</td>
</tr>
<tr>
<td>Haiti**</td>
<td>65</td>
<td>0.8</td>
<td>159</td>
<td>0</td>
<td>1</td>
<td>159</td>
<td>0</td>
<td>D6 (endemic)</td>
</tr>
<tr>
<td>United States*</td>
<td>NA</td>
<td>NA</td>
<td>109</td>
<td>0</td>
<td>10</td>
<td>3–14</td>
<td>9 (90)</td>
<td>Imported (D7, D5, D3, H1)</td>
</tr>
<tr>
<td>Venezuela**</td>
<td>1544</td>
<td>6.2</td>
<td>113</td>
<td>9</td>
<td>1</td>
<td>104</td>
<td>1 (100)</td>
<td>D9 (imported)</td>
</tr>
</tbody>
</table>

NOTE. NA, not applicable.

* Countries with reported endemic transmission in 2000.

** No. of discarded cases is an approximate minimum based on the no. of measles IgM-negative cases reported each year.

*** The first cases may have been imported. Dominican Republic had measles circulation after 1999 and shares a large border with Haiti.

** The first case of the outbreak was reportedly a traveler from Europe.

Methodology for house-to-house monitoring. The 95% coverage level required to maintain the interruption of indigenous measles transmission means, in practical terms, that all (or almost all) children must be vaccinated. An overseer could rapidly assess the completeness of the vaccination effort at the local level by visiting a limited number of houses with 1- to 4-year-old children and asking for evidence of their prior vaccination with a measles-containing vaccine (figure 2). To decrease the likelihood of missing problem areas (thus wrongly concluding that the neighborhood is well vaccinated when it is not), the overseer is encouraged to select a total of four blocks far away from the health center in zones that are difficult to access or underserved, have a high proportion of recent migrants of rural origin, or where recent cases have been reported. It is important that a member of the local staff directly involved in vaccination accompanies and assists the overseer in this task, thus becoming a direct witness to the monitoring process. This person should not participate in the choice of blocks or houses to be visited.

Starting in a corner of the block chosen, the team moves from one door to the next nearest one until five houses with 1- to 4-year-old children for whom immunization information is available are visited. The same procedure should be followed for the remaining three blocks. A child is considered vaccinated if the vaccination is recorded on the vaccination card. In some countries (e.g., Haiti), where vaccination cards are not always updated during door-to-door vaccination, verbal confirmation of vaccination by the parents or caretakers is also accepted during campaigns. If unvaccinated children are found, the monitors should ask parents to explain why the children are not vaccinated. If
the adult responsible for providing the card is absent or if it is convincingly shown that the vaccination card is kept elsewhere (e.g., the child does not live there), the household is excluded from the sample and not registered on the chart.

The monitoring ends when a total of 20 houses with eligible children have been visited. Because it would be very unlikely to find many houses with eligible unvaccinated children in a well-vaccinated neighborhood, the finding of a total of two houses with at least 1 nonimmunized child each (even before 20 houses are visited) is reason enough to stop monitoring immediately and consider that vaccination efforts in that neighborhood were ineffective.

The finding of unvaccinated children plus the information gathered from parents will be the basis for providing feedback to the local vaccination authorities as to the necessity and methods to improve immunization in the area. For this feedback to strengthen the vaccination program at the local level, house-to-house monitoring should be done regularly during all supervisory visits and should be followed by specific recommendations.

Supervision during campaigns. In addition to routine vaccination, countries rely on periodic national vaccination campaigns (i.e., follow-up campaigns) and mop-up operations to achieve the interruption of indigenous measles transmission. These campaigns can be affected by a number of problems, including the lack of proper day-to-day supervision and inappropriate definition of territories to be vaccinated.

During door-to-door campaigns, the supervisors should verify daily that the vaccination teams visited all houses in the selected sector by checking that the doors of all houses were correctly marked by them. During both door-to-door and fixed-post campaigns, house-to-house monitoring should be performed by a selected team of overseers once vaccination in a neighborhood or health sector is considered done by the program managers. Its findings, including the proportion of children unvaccinated and reasons for a lack of vaccination, will be the main tools used to define if the work in that neighborhood was indeed finalized or needs to be redone. Monitoring results are more reliable if the monitors are not the same people who were responsible for vaccination in that neighborhood or health sector. Some countries (e.g., Bolivia, Dominican Republic, Haiti, Paraguay, and Venezuela) have used overseers from the national and provincial level. Bolivia and Ecuador have successfully used the program managers responsible for vaccination in one health sector as monitors for another.

Adjustment and validation of population denominators. Ad hoc adjustments of coverage data by selecting alternative denominators appropriate for the area may also be used. In areas with high rates of institutional births, the denominator “population aged <1 year” could be replaced by the number of bacille Calmette-Guérin (BCG) doses administered to infants (coverage for the year = no. of doses of a measles-containing vaccine administered to 1-year-old children divided by the number of BCG doses administered to infants during the same year).

In areas with low rates of institutional births but high coverage with the first dose of diphtheria-tetanus toxoids–pertussis (DTP) vaccine, a better replacement for the denominator might be the number of first doses of DTP administered to infants.

Use of birth registries. In some countries (e.g., Guatemala), in order to get birth registration the parents must show the vaccination card with the first doses already registered, and health centers use the yearly number of births to validate their population denominator. In that way they establish the target population and set parameters (Tabla de Salvación) for the monthly vaccination of ~8.4% of the population that is <1 year of age. Coverage is measured monthly at this level. In addition, coverage data are centralized and analyzed at the provincial level to determine monthly which areas are at risk for low coverage and which ones among them will need mop-up operations. This method could help to both improve vaccination coverage and validate census information. Nonetheless, not all births are registered and some are registered with important delays, and misclassification of children who migrate within the first year of life also occurs.

Universal birth and vaccination registry. The reference standard for validating routine coverage is a universal registry that includes the whole birth cohort. Such a system has been used in Uruguay since the 1980s. In brief, all newborns are registered in a national database that is also used for immunizations. This is updated electronically every time the child receives a new vaccination. Although highly accurate, data entry for this system is still highly centralized; thus, data are not immediately available at the local level for the day-to-day monitoring of undervaccinated children. A project is ongoing to decentralize the system.

Zonification (Canalizaciones). Another useful method is
to divide the municipality by neighborhoods or groups of blocks and place each one under the responsibility of a nurse or a primary health care worker (health agent). This worker must visit all houses in the neighborhood a number of times per year (usually up to 3) to provide vaccinations and other preventive services. When well implemented and supervised, this strategy can help underserved areas reach universal coverage for vaccination, prenatal care, and other services. Variations of this strategy have been used in Cuba, in some areas of Colombia, Bolivia, Brazil, and other countries. Nonetheless, it is labor-intensive and needs close supervision.

**Drop-out rates.** In areas with a stable, low-migration population, where vaccination coverage does not vary substantially between years, the DTP1-measles drop-out rate (i.e., [no. of first doses of DTP administered to children <1 year of age — no. of first doses of measles vaccine given to 1-year-old children/no. of first doses of DTP administered to children <1 year of age]) could also provide useful insights as to the proportion of children lost by the system. In countries where health centers keep reliable records, a review of vaccination records at the center can provide very valuable information on drop-out rates.

**OUTBREAK INVESTIGATIONS AND SURVEILLANCE**

**Quality of outbreak investigations.** Because measles can be transmitted through aerosolized particles, an infectious individual can transmit the virus to persons near and far away [4]. Also, the virus can remain in the air and remain infectious after the infectious person has left the room, thus allowing transmission even to people with whom this person has had no direct contact (e.g., transmission in hospital waiting rooms, public places, and on public transport systems). Therefore, the thorough investigation of all contacts and places visited by the patient during the 7–18 days before rash onset is essential in order to identify who could have transmitted the disease to a new patient and where and when transmission could have occurred (figure 3) [5]. Also, the investigation of all contacts and places visited by the patient during the period between the first respiratory symptoms until 4 days after rash onset becomes fundamental in determining the existence of secondary transmission (figure 3). Moreover, because 7–18 days will elapse between contact with an infectious person and rash onset in the secondary case, repeated visits to persons who may have been exposed and repeated active-case searches are required for the investigation of a measles case to be considered complete.

Serum samples should be obtained from the first 5–10 suspected cases of each outbreak during the first visit to a health provider to detect measles IgM. To be useful, these samples should be obtained within 30 days after rash onset. Also, nasopharyngeal, oropharyngeal, or urine specimens should be obtained within 7 days after rash onset to identify the responsible virus. Obtaining viral specimens from all outbreaks is crucial to assess the interruption of indigenous transmission.
The virus genotype can identify a foreign virus or the continuing circulation of an indigenous strain. In the absence of indigenous transmission, all outbreaks should be import-related. Therefore, a timely and adequate investigation of all outbreaks in countries without indigenous transmission (including taking specimens for virus isolation) should establish the link to an imported case in most outbreaks investigated (table 1).

Regarding outbreak size, the experience from Chile, Uruguay, Bolivia, Brazil, and other countries during the last 3 years showed that outbreaks reaching ≥25 cases often reveal important risk factors for disease transmission that, if not appropriately controlled, could allow indigenous transmission to resume. Also, local vaccination coverage data, adjusted as appropriate, should be obtained and door-to-door monitoring of vaccination should be done in the neighborhood of residency and in all municipalities visited by the case-patient during the exposure and infectious periods. The information thus obtained should be summarized in an outbreak investigation report form (the form can be found on the Web at http://www.paho.org); this should allow the epidemiologist to determine the outbreak duration and size, its link to importations, the age groups most affected, the proportion of vaccinated cases by age, and the vaccination status in the area. This information is vital to assess whether indigenous transmission exists and to guide public health authorities as to the most appropriate control measures, including the decision to conduct mop-up operations, how extensive they should be, and which age and risk groups should be vaccinated.

**Surveillance indicators.** Because of the clinical similarities between measles and rubella, because most countries in the Region already use measles- and rubella-containing vaccines (mostly measles-mumps-rubella vaccine) in their routine program, and because the control of rubella and congenital rubella are priorities for the Region, PAHO recommends the integration of measles and rubella surveillance.

No surveillance system can detect all cases. Moreover, imported cases are often overlooked: Visitors do not always seek medical care locally, and those who do often go to private practitioners, who are less likely to report cases. Therefore, a very sensitive system is needed to detect cases in countries where indigenous transmission is low or absent. Such a system requires that the quality of surveillance be regularly monitored and validated.

Even in the absence of suspected or confirmed measles or rubella cases, all health centers in PAHO’s sentinel surveillance system should report weekly. The weekly reporting rate, calculated as the proportion of the reporting health centers that sent their surveillance report in time, even in the absence of cases, was successfully used to eradicate poliomyelitis and is an effective tool for assessing surveillance compliance at the local level. The quality of the data reported should also be monitored.

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**Figure 3.** Household census chart used for the investigation of measles cases and their contacts in the Region of the Americas.
weekly. This includes the percent of investigations that included a visit to the patient’s home made within 48 h of notification of a suspected case, the percent of suspected cases with a blood sample obtained within 30 days after rash onset, the percent of samples received by the reference laboratory within 5 days after being obtained, the percent of laboratory results reported within 4 days after receipt of the sample, and the percent of cases discarded on the basis of a laboratory test. PAHO recommends 80% compliance with all indicators. They are monitored weekly through the publication of a weekly measles bulletin that provides information from all countries of the Region. Although an expected baseline for the incidence of acute flaccid paralysis in the absence of poliomyelitis is widely utilized, no such baseline is available for suspected cases of measles or rubella. In the Region, such rates can vary between <1 and 40 per 100,000 (table 1). Nonetheless, the proportion of discarded cases per 100,000 population reported to the PAHO integrated measles-rubella surveillance system is useful for comparing the surveillance sensitivity between municipalities with similar demographic and geographic characteristics. It also permits the assessment of sensitivity of the surveillance system over time in the same geographic area.

ACTIVE-CASE SEARCHES

The main surveillance validation tool used by PAHO is active-case search. Active-case searches should be performed regularly in silent (those not reporting weekly) and underserved areas and in areas where cases have been identified, areas with high rural-to-urban migration, or areas often visited by tourists. Case searches should be implemented in health centers, hospitals, and private clinics and at the workplace, schools, preschools, and other educational institutions. The case search is usually limited to cases that occurred within the 30 days preceding the investigation because viable serum samples can still be obtained from the patients to confirm the diagnosis.

Case searches at health care institutions. The investigators visit health centers, hospitals, and private clinics and practices and interview all health care personnel and statisticians, asking them for suspected cases of measles or rubella or cases of rash and fever seen within the previous month. Because most practitioners have never seen a measles case in their practice, it is recommended to show them a picture of a case and remind them of its main clinical characteristics. After the interviews, the investigators check the outpatient, emergency room, and hospitalization records, looking for unreported rash and fever cases. If a suspected case is found, the investigators should record all information available, visit the patient’s home, and perform a full case investigation, including obtaining a serum, nasopharyngeal, or urine specimen as appropriate. At the end of the visit, the investigators should discuss the problems detected with the staff, provide them with up-to-date information on how to report suspected cases, encourage them to report, and provide them with report forms. Pictures of measles cases and descriptions of the main characteristics of the disease and the phone number to call if cases are found should also be hung in readily visible places.

Case Searches at Schools

These active-case searches serve a dual public health and education purpose. The visitors, usually epidemiologists and other local public health personnel, explain class-by-class the main characteristics of measles, using either a picture of a measles case or by making a blackboard drawing of a child sick with measles. They then briefly discuss the role of vaccination in measles prevention and ask the students if they know of recent cases either at school or in their neighborhood. Each class visit usually takes 10 min. If the students report a case compatible with measles, the investigators should visit the house of the person suspected of having measles, perform the investigation, and obtain a serum sample. In well-conducted searches, the investigators might find as many as 1 suspected case per school.

DISCUSSION

The interruption of indigenous measles transmission in the Region of the Americas in the absence of global eradication is challenging. Without a perfect vaccine that protects 100% of those vaccinated, wild measles infections will continue to occur due to importations from countries where the disease is endemic, even if coverage is ≥95%. In such cases, all outbreaks should be related to importations (i.e., the index case should be imported), and disease transmission originating from these importations should quickly die out. Therefore, the absence of indigenous transmission means that, without intervention, the outbreaks will be self-limited, and the average number of secondary cases (R) produced by a typical imported case in a given population should be <1 [6]. This can be estimated by using either the proportion of imported cases (for R < 1, R = 1 − the proportion of imported cases) or the average outbreak size. There are, nonetheless, practical limitations to estimating R for an immunization program in the Region of the Americas. First, susceptibility patterns can vary substantially among different risk groups (even within the same outbreak, a different estimate of R should apply for each group). Second, PAHO recommends immediate, large-scale mop-up vaccination (usually including all children <5 years of age in the affected area or municipality) for outbreak control purposes in areas where vaccination coverage is <95%. This intervention can modify transmission and affect the true estimate of R, particularly if it is done early after the beginning of the outbreak. Last, the estimate of R in coun-
tries with few outbreaks each year, which is the case in most countries in the Region (table 1), is often unreliable.

Poor-quality coverage information due to inaccurate denominator data is an important problem, particularly in rural areas that lose population due to migrations not forecast by the census and in the highly populated urban settings that attract migrants. Therefore, a systematic bias often occurs that underestimates coverage in underserved rural areas and overestimates it in heavily populated cities. Moreover, even if data at the provincial or municipal level were reliable, these aggregated data often hide important inequalities at the local level, where the most disadvantaged people (who would benefit more from vaccination) usually have the lowest real coverage [7]. As shown by others, rigorous monitoring is the key to the success of disease-control initiatives [8]. The supervisor’s use of routine house-to-house monitoring to assess if the eligible children have been vaccinated is time- and cost-efficient (it usually takes <2 h of the supervisor’s time). The adjustment and validation of population denominators through selecting alternative denominators (DTP1 or BCG coverage), using universal registries, corrected birth registries, or drop-out rates, can be useful depending on local characteristics. The decision to use any combination of these tools to independently verify the vaccination status of the community and assure accountability of the local vaccine program managers relies on the supervisor’s experience. Nonetheless, assessing coverage will not, by itself, resolve the problem. Local vaccine program managers should be given the authority and resources needed to efficiently perform their work; otherwise, supervision becomes a futile exercise.

In the absence of a 100% specific confirmatory test, some suspected measles cases will be laboratory-confirmed even in countries without real measles transmission and no imported cases. These “confirmed” cases will be either false-positives (because of errors inherent to a less than 100% specific confirmatory test) or true IgM positives due to a recent measles vaccination in a person that otherwise has no wild measles infection. Because these “sporadic” confirmed cases will continue to occur, PAHO emphasizes the importance of a thorough case investigation, including visiting households, obtaining samples and specimens for laboratory analysis, and performing coverage monitoring and active-case searches.

To reach, maintain, and assess the interruption of indigenous measles transmission, countries in the Region of the Americas should follow all PAHO recommendations. These include (1) following the recommended vaccination strategies, reaching 95% coverage by municipality; (2) monitoring coverage house-to-house at the local level during supervisions, vaccination campaigns, and mop-up operations, and implementing corrective measures immediately if insufficient coverage is found; (3) investigating all cases and outbreaks within 48 h of reporting, following the guidelines described above; (4) performing routine measles surveillance and validating compliance on a weekly basis using PAHO indicators; and (4) performing regular active-case searches for surveillance validation.

Full compliance with these recommendations will ensure that countries of the Region achieve and maintain the interruption of indigenous measles transmission for as long as necessary until global eradication is achieved.

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References