The 24th Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30 am to 4:30 pm on November 10, 2015 to discuss the potential eradicability of measles and rubella. The Task Force members at the time of this meeting were Sir George Alleyne, Johns Hopkins University; Dr. Stephen Blount, The Carter Center; Dr. Dirk Engels, World Health Organization (WHO); Dr. Donald Hopkins, The Carter Center (Chair); Dr. Julie Jacobson, Bill & Melinda Gates Foundation; Dr. Adetokunbo Lucas, Harvard University; Dr. Patrick Osewe, The World Bank; Professor David Molyneux, Liverpool School of Tropical Medicine (retired); Dr. Mark Rosenberg, Task Force for Global Health; Dr. Laurence Slutsker, Centers for Disease Control and Prevention (CDC); Dr. Harrison Spencer, Association of Schools of Public Health; Dr. Roberto Tapia, Carlos Slim Foundation; Dr. Ricardo Thompson, National Institute of Health (Mozambique), and Dr. Dyann Wirth, Harvard School of Public Health. Seven Task Force members (Blount, Hopkins, Lucas, Osewe, Rosenberg, Slutsker, Thompson, Wirth) attended this meeting (Hopkins by telephone), and one was represented by an alternate (Dr. Steve Ault for Engels). Dr. Henri van den Hombergh represented UNICEF, which has not yet appointed a new Task Force member since Dr. Mickey Chopra left UNICEF in August 2015.

Presenters at the meeting, which was chaired by Dr. Stephen Blount, included Dr. Paul Rota, Centers for Disease Control and Prevention; Dr. Peter Strebel, World Health Organization; Dr. Kimberly Thompson, Kid Risk, Inc. and University of Central Florida College of Medicine; Dr. Peter Figueroa, University of the West Indies, and Dr. Jon Andrus, Sabin Vaccine Institute.

**Measles Eradication**

The ITFDE previously considered this topic in June 2009, when it concluded that “measles eradication is biologically possible, using tools that are currently available, as already demonstrated in the Americas,….[but that] the delay in eradication of polio is a special obstacle to global measles eradication”.¹ The ITFDE reviewed the current status of global measles elimination and rubella control and regional elimination at this meeting, with

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particular emphasis on the potential advantages of pursuing measles and rubella eradication simultaneously, and the constraints of insufficient resources and political commitment that are impeding progress.

Measles is one of the most infectious diseases known, and it confers life-long immunity on persons who recover from the infection. The virus is transmitted from person-to-person by respiratory droplet nuclei spread or by direct contact with infected nasal or throat secretions. Patients are most infectious during the four-day prodromal period just before the characteristic rash appears and continue to shed virus for another four days after the rash appears. Transmission occurs year-round, but normally peaks in the dry season or late winter/early spring, with major epidemics appearing at 2-4 year intervals. There is no animal reservoir of infection, and no asymptomatic carrier state. Measles virus is monotypic, genetically stable and shows no evidence of genetic recombination.

Before live attenuated measles vaccine was licensed in 1963, measles killed an estimated more than 2 million children globally each year. With increasing immunization coverage, the number of estimated deaths from measles globally was reduced to about 550,000 in 2000 (routine immunization coverage of 72%), and to 115,000 deaths by 2014 (85% coverage).

The attenuated live measles vaccine is highly effective, yielding seroconversion rates of 95% or more in persons over 12 months old, is administered by subcutaneous or intramuscular injection, and must be refrigerated. The vaccine is less effective in infants under 12 months of age (e.g., 85%-90% seroconversion in 9-month-olds and 50%-60% in 6-month-olds). Infants become susceptible to the disease at differing times due to the loss of maternal antibodies (which protect younger infants from infection), as well as because of their own immunological immaturity. Hence, some infants are exposed to and infected by the wild measles virus before they are immunized effectively by vaccination. The routine measles vaccination regimen is two doses. WHO recommends that in countries with ongoing measles transmission in which the risk of measles mortality among infants remains high, the first dose (MCV1) should be administered at age 9 months, while in countries with low rates of measles transmission MCV1 may be given at 12 months. Those countries that give MCV1 at age 9 months should administer MCV2 at age 15-18 months; countries which give MCV1 at 12 months have the option of administering MCV2 at 15-18 months or at school entry depending on programmatic considerations.1 Almost all children who fail to respond to the first dose of measles vaccine will respond to the second dose. Seroconversion rates after two doses are usually greater than 95% if the first dose is given at 9 months and greater than 99% if the first dose is given at 12 months or older. Providing all children with at least 2 doses of measles vaccine is now the standard for all national immunization programs and has been WHO policy since 2009, with the second dose delivered either through campaigns or through routine health services depending on which approach reaches the highest coverage.

In 1994, the World Health Organization region of the Americas (AMR) was certified as free of indigenous polio and immediately established a regional goal to eliminate measles by the year 2000. The operational strategy used included “catch-up” mass measles immunization campaigns that initially targeted all children 9 months-14 years of age, regardless of immunization or disease history, in order to quickly raise immunization levels to 90% or more. Programs then sought by means of adequate routine immunization to “keep-up”, maintaining high immunization levels in the face of continuing new births (susceptibles). Those efforts were supplemented as needed by “follow-up” campaigns about every four years targeting 1-4 year-olds, in order to ensure first measles immunizations to children who had been missed by routine immunization services, and simultaneously deliver a second dose of measles vaccine to young children who had already received their first dose.

Most American countries conducted “catch up” campaigns between 1989 and 1998, and “follow up” campaigns starting in 1996. Many American countries had already stepped up measles immunization by including it with polio immunization during the latter years of the regional campaign to eliminate polio. The last endemic cases of measles in the Americas occurred in Venezuela in November 2002. More recently, in 2014, measles reestablished transmission in eastern Brazil for a period of 15 months, following importation in December 2013. Since July 2015 Brazil has once again is free of endemic measles. In addition to high levels of performance on epidemiologic surveillance, and laboratory diagnosis, “keep up” (routine) and “follow up” immunizations have been required to prevent the numerous cases of measles imported from other regions from re-establishing endemic transmission in the Americas. Other noteworthy elements of the success in the Americas include high levels of political support and relatively high routine immunization levels in the countries, vaccine laws to ensure funding as a line item for immunization in national budgets, and a special Vaccine Revolving Fund that the Pan American Health Organization (PAHO) established to facilitate advantageous procurement and timely availability of measles vaccine. In 2003, PAHO established a new goal of eliminating rubella and congenital rubella syndrome from the Americas by 2010, which was achieved in 2009, using measles- and rubella-containing (MR) vaccine. In April 2015, the Americas became the first WHO region to be verified by an independent commission as rubella free. Experience from the Americas demonstrates that use of MR (or measles, mumps, rubella [MMR]) vaccine as the standard of care in both routine immunization and mass campaigns was mutually reinforcing in sustaining interruption of both measles and rubella virus transmission.

Worldwide progress toward regional measles elimination has been recently reviewed. In 2000, the United Nations General Assembly adopted the Millennium Development Goals (MDG), with MDG4 being a two-thirds reduction in child mortality by 2015, and with measles vaccination coverage being one of the three indicators of progress toward this goal. In 2010, the World Health Assembly established three milestones for measles control by 2015: 1) increase routine coverage with the first dose of measles-containing vaccine

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2 Additional information available at [http://www.unmillenniumproject.org/goals/phi.htm#goal4](http://www.unmillenniumproject.org/goals/phi.htm#goal4)
(MCV1) for children aged 1 year to ≥90% nationally and ≥80% in every district; 2) reduce global annual measles incidence to <5 cases per million population; and 3) reduce global measles mortality by 95% from the 2000 estimate.1,2 In 2012, the World Health Assembly endorsed the Global Vaccine Action Plan3 with the objective to eliminate measles in four World Health Organization (WHO) regions by 2015. WHO member states in all six WHO regions have adopted measles elimination goals with targets of 2020 or earlier. During 2000-2014, annual reported measles incidence declined 73% worldwide, from 146 to 40 cases per million population, and annual estimated measles deaths declined 79%, from 546,800 to 114,900. However, since 2010, progress towards the 2015 WHA goals slowed markedly.

During 2000–2014, increased coverage worldwide with both (1st and 2nd) routine doses of MCV, combined with supplemental immunization activities (SIAs) in countries that lack high coverage with 2 doses of MCV, contributed to the 73% decrease in reported measles incidence and 79% reduction in estimated measles mortality (Table 1). During this period, measles vaccination prevented an estimated 17.1 million deaths. However, on the basis of current trends in measles vaccination coverage and incidence, the WHO Strategic Advisory Group of Experts on Immunization concluded that the 2015 global milestones and measles elimination goals will not be achieved. To resume progress toward these milestones and goals, a review of current strategies and challenges to improving program performance is needed, and countries and their partners need to raise the visibility of measles elimination, address barriers to measles vaccination, and make substantial and sustained additional investments in strengthening health systems.

Measles can serve as an indicator of the strength and reach of the health system, as measles outbreaks reveal populations poorly served by health services. In high-burden, low-coverage countries, outbreak investigations have identified several policies or practices associated with low MCV1 coverage including: 1) recommending not to routinely vaccinate children aged ≥12 months; 2) discouraging the opening of a 10-dose vial when few children are present; and 3) limiting measles vaccination at routine EPI clinics to only one session per month (Global Immunization Division, Center for Global Health, CDC, unpublished data, 2015). Addressing these gaps, maximizing how SIA planning and implementation can improve routine services, and conducting high-quality SIAs should increase coverage and equity for all vaccines and further reduce the number of measles cases and deaths. Where adequately supported and encouraged, countries might schedule

2 Whereas the coverage milestone is to be met by every country, the incidence and mortality reduction milestones are to be met globally.
3 The Global Vaccine Action Plan is the implementation plan of the Decade of Vaccines, a collaboration between WHO, UNICEF, the Bill & Melinda Gates Foundation, Gavi, the Vaccine Alliance, the U.S. National Institute of Allergy and Infectious Diseases, the African Leaders Malaria Alliance, and others to extend the full benefit of immunization to all persons by 2020 and beyond. Additional information is available at http://www.who.int/immunization/global_vaccine_action_plan/en and at http://apps.who.int/gb/ebwha/pdf_files/wha65/a65_22-en.pdf.
SIAs more as PIRIs (Periodic Intensification of Routine Immunization) so as to increase readiness and reduce collateral negative effects on the routine systems. As coverage improves, establishing a visit during the second year of life integrating MCV2 and other child health interventions should help to further reduce measles burden.

The decrease in measles mortality is among the main contributors (along with decreases in pneumonia, diarrhea, and malaria) to the decline in overall child mortality and progress toward MDG4. To assess the reasons for the slowing of progress since 2010 and to modify current strategies as needed, the Measles and Rubella Initiative 1 partners have commissioned a midterm strategy review.

Great concern was expressed during the meeting about decreases during 2008-2012 in funding due largely to Gavi’s exit during this period as a funding organization, and wavering political commitment for measles immunization and related efforts which have contributed to a slowing in progress toward measles elimination. The return of Gavi funding since 2012 and an increase in its commitment for measles and rubella immunization during the 2016-2020 period from US$ 600 million to US$ 820 million is encouraging. To help regain momentum and accelerate progress, transitioning of the polio infrastructure and assets to measles and rubella eradication is a natural fit for several reasons including: 1) the strategies are similar—surveillance, achieving and maintaining high routine immunization coverage, periodic mass campaigns to reach unreached children; 2) polio assets are concentrated in the lowest-performing countries with the weakest immunization systems, which are the same countries with most of the measles cases and deaths and the greatest challenges, and 3) redirecting these assets for measles and rubella eradication would help to maintain essential polio functions that need to continue after polio eradication.

The economic literature and the measles-rubella investment case demonstrate that: 1) “high control” is not cost effective if eradication is feasible; 2) successful eradication would be considerably less costly both in human and financial terms over the longer term than control and represents a better health and financial option; 3) outbreaks are very expensive and inefficient to control and terminate4,5,6. With polio eradication nearing completion, the

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1 The Measles & Rubella Initiative is a partnership established in 2001 as the Measles Initiative, led by the American Red Cross, CDC, the United Nations Foundation, UNICEF, and WHO. Additional information is available at http://www.measlesrubellainitiative.org.
opportunity exists to position measles and rubella elimination as the highest disease control priority within the Global Vaccine Action Plan and to instill real accountability for achieving these goals. The role of WHO in this context should be to strengthen and promote coordination among regions and within countries between polio and measles-rubella initiatives.

**Rubella Eradication**

Rubella virus usually causes a mild fever and rash in children and adults. However, infection during pregnancy, especially during the first trimester, can result in miscarriage, fetal death, stillbirth, or a constellation of congenital malformations known as congenital rubella syndrome (CRS). Rubella virus is the leading vaccine preventable cause of birth defects. Globally, over 100,000 infants are born with CRS each year, mostly in low income countries that have not introduced RCV. In 2011, the World Health Organization (WHO) updated guidance on the preferred strategy for introducing rubella-containing vaccine (RCV) into national routine immunization schedules, including an initial vaccination campaign usually targeting children aged 9 months–15 years. Rubella vaccine-induced immunity is generally assumed to be lifelong. The Global Vaccine Action Plan endorsed by the World Health Assembly in 2012 and the Global Measles and Rubella Strategic Plan (2012–2020) published by Measles and Rubella Initiative partners in 2012 both include goals to eliminate rubella and CRS in at least two WHO regions by 2015, and at least five WHO regions by 2020. A recent report summarizes global progress toward rubella and CRS control and elimination during 2000–2014. As of December 2014, RCV had been introduced in 140 (72%) countries, an increase from 99 (51%) countries in 2000 (Table 1). Reported rubella cases declined 95%, from 670,894 cases in 102 countries in 2000 to 33,068 cases in 162 countries in 2014, although reporting is inconsistent. To achieve the 2020 Global Vaccine Action Plan rubella and CRS elimination goals, RCV introduction needs to continue as country criteria indicating readiness are met, and rubella and CRS surveillance need to be strengthened to ensure that progress toward elimination can be measured.

Since 2012, the Gavi Alliance opened a new window of funding for rubella vaccine introduction by Gavi-eligible countries, pledging more than $500 million, and introduction of RCV into immunization schedules has accelerated. RCV needs to be introduced in countries as WHO criteria for introduction are met. Gavi Alliance funding support is instrumental in ensuring continued RCV introduction. Forty-two (78%) of the 54 countries where RCV is not in the national immunization schedule are eligible for Gavi Alliance funding support. Leadership, coordination, technical expertise, and financial resources provided by the Measles and Rubella Initiative partners also have provided critical support to accelerate RCV introduction in more countries and increase global RCV coverage.

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Recent and future RCV introductions provide an opportunity to establish and achieve regional rubella and CRS elimination goals. During 2012–2014, a rubella elimination goal was established in the Western Pacific Region, and a goal to control rubella and CRS was established in the South-East Asia Region as an initial step toward establishing an elimination goal. The interruption of rubella virus transmission announced in April 2015 in the Region of the Americas provides evidence that rubella and CRS elimination can be achieved by introduction of rubella vaccine into routine childhood vaccination schedules accompanied by a wide age range (i.e., infants to 15 years, and in some cases up to 39 years) immunization campaign. However, key challenges to achieving rubella elimination goals include civil unrest (Eastern Mediterranean Region), weak health care delivery systems with low routine vaccination coverage (African and South-East Asia Region), and sub-optimal acceptance rate (European Region). It is recognized that routine immunization services in the Americas are stronger than in most other WHO regions.

High-quality rubella and CRS surveillance is needed to monitor the impact of rubella vaccination programs, and verify achievement of rubella and CRS elimination goals. Guidelines for rubella and CRS surveillance\(^1\), and a framework for verifying elimination of rubella and CRS have been published.\(^2\) Countries need to institute CRS surveillance and report both rubella and CRS cases to WHO at least monthly. There has been a recent decrease in the number of countries reporting their rubella and CRS cases which is particularly concerning regarding the attention given to monitoring control and elimination goals.

A vaccine delivery system that achieves and maintains high coverage with both MRCV and MCV and integrated measles and rubella surveillance is a necessary foundation for continued progress toward measles elimination and rubella and CRS control and elimination. Implementation of additional global WHO recommendations regarding the use of RCV can help countries that have introduced RCV optimize their use of the vaccine.\(^3\) The recommendations include adding RCV to measles vaccine when the latter is administered in routine immunization services for vaccination of health workers; addition of use of RCV to all measles campaigns; and a review of measles and rubella epidemiology to determine target age ranges. In addition, the recommendations include improved monitoring of activities reflecting RCV use, including joint measles and rubella vaccination coverage surveys and regular analysis of measles and rubella surveillance data. Such analyses are needed to identify geographic areas and population groups with low immunity who are at greater risk for outbreaks, so that vaccination campaigns and other prevention and control measures can be directed toward them.


\(^3\) WHO. Meeting of the Strategic Advisory Group of Experts on Immunization, November 2013 Meeting-conclusions and recommendations: *Wkly Epidemiol Rec.* 2014 Jan 3;89(1).
Immunization and surveillance activities are the foundation for rubella control/elimination and CRS prevention/elimination and reaching the Global Vaccine Action Plan goals. To reach regional elimination goals, countries at all levels need to follow the WHO recommendations for introducing RCV, strengthening routine immunization services, improving surveillance, and accelerating coordinated rubella control and elimination efforts.

Conclusions and Recommendations

1. At the beginning of this century, measles was one of the five leading killers of children with an estimated 546,800 annual deaths. Since then, with some support from the Measles and Rubella Initiative (M&RI), there has been remarkable progress with a 79% reduction in deaths to 114,900 in 2014. However, this continuing death burden is unacceptable given the availability of a highly effective and inexpensive vaccine ($0.25 per dose through UNICEF) for more than 50 years.

2. Rubella virus is the leading infectious cause of congenital birth defects. Remarkable progress has been achieved in introducing use of this vaccine in developing countries and reducing the global inequity in its use, as well as in the numbers of reported cases of rubella and of CRS. Use by countries in their routine childhood immunization schedules has increased from 99 (51%) countries in 2000 to 140 (72%) countries in 2015, and the Region of the Americas has interrupted endemic rubella transmission since 2009.

3. Efforts to control and eliminate measles and rubella have accelerated incrementally since 2000, but have been greatly overshadowed in magnitude of resources and political commitment by the global polio eradication initiative (GPEI). The impending completion of polio eradication opens a window of opportunity to devote greater attention to measles and rubella eradication. Since 2012 GAVI has opened funding windows for rubella vaccine introduction into GAVI-eligible countries, and measles follow-up SIAs in high burden countries, pledging $820 million for the period 2016-2020 for measles and rubella immunization.

4. The high level of measles and rubella control that has been attained already has significantly reduced deaths from measles and cases of congenital rubella syndrome, which is a major accomplishment, but a paradigm shift will be needed in order to eradicate measles and rubella. Eradication will require a much more demanding enterprise than the current effort, which has suffered from insufficient resources and wavering political commitment.

5. There is currently no global commitment to eradicate measles or rubella, although all six regions of WHO, through their regional committees, have now agreed to eliminate measles by no later than 2020; for rubella, two regions have set an elimination goal. The ITFDE encourages discussion of the feasibility and potential timing of such a global commitment in countries, in each WHO region and at the World Health Assembly.
6. The ITFDE still firmly believes that both measles and rubella eradication are technically feasible, but the very high contagiousness of measles is the biggest challenge to success, and measles and rubella eradication would require a sustained global commitment and a clear accountability framework such as exists for GPEI.

7. Careful consideration should be given to how best to blend the scaling up of interventions against measles and rubella with the scaling down of the polio eradication initiative, in order to maximize benefits to both efforts. Countries should adapt infrastructure and resources developed for polio eradication for measles and rubella eradication; conversely measles and rubella eradication infrastructure could help to support high quality surveillance and any supplemental immunizations needed to detect, investigate and contain imported or suspected cases of polio in the future.

8. Strategies and plans for eliminating measles and rubella must be developed and adapted by individual countries and WHO regions, with appropriate attention to innovative strategies, local circumstances, capacities and cultures. Each national program should engage local communities in determining how best to obtain and sustain high immunization coverage and prompt reporting of cases.

9. Because of the high contagiousness of measles, strengthened routine immunization services may be required in order to attain and maintain the unusually high immunization levels and prompt immunization of new birth cohorts that are needed for measles eradication, much more so than was necessary for smallpox or polio eradication. The occurrence of measles outbreaks can and should be used as an indicator of well (or poorly) performing routine immunization services and as a means to target countries and high risk areas in need of efforts to improve routine immunization coverage. The polio eradication program has learned a lot about reaching children who are normally missed by routine immunization efforts, and country immunization programs should use this knowledge.

10. Measles eradication demands support for an accelerated and prioritized research agenda, including improved tools for immunization, diagnosis, and rapid assessment of immunity; and operational research to improve surveillance and reporting, as well as delivery of vaccines. The thermostable microneedle patch for delivery of measles and rubella vaccine seems especially promising and innovative but urgently needs funding for clinical testing.

11. The economic literature and the measles-rubella investment case confirm that eradication is more cost effective than indefinite control.

12. Combining immunization against rubella along with measles immunization using measles-rubella (MR) vaccine could eliminate rubella even sooner than measles because of its lower transmissibility, thus providing an enormous additional benefit at relatively small marginal cost.

13. For operational purposes, the campaign to stop measles transmission should focus on the numbers of incident cases remaining, not on rates of cases per population or on reductions in deaths, since the goal is to get to zero indigenous cases. The latter measures are more appropriate for advocacy, not for running a program.

14. Advocacy for eradication of measles and rubella would be improved by:
a. strengthening the investment case for eradication;
b. recognizing the significance of eradication as a public health and social movement, an issue of equity;
c. linking eradication to the Global Health Security agenda;
d. establishing a robust strategy to communicate the urgency of eradication to decision makers; and

e. identifying champions for eradication, particularly from countries bearing the greatest disease burden.
### Status of Measles and Rubella Elimination by WHO Region

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Coverage as of 2014</th>
<th>Reported Measles Cases 2014</th>
<th>Reported Rubella Cases 2014</th>
<th>Target Years for Elimination Measles/Rubella</th>
<th>Salient Challenges</th>
</tr>
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<tbody>
<tr>
<td>Americas</td>
<td>MCVI 92% MCV2 51%</td>
<td>1,817</td>
<td>4</td>
<td>2000/2010</td>
<td>Importations</td>
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<tr>
<td>Europe</td>
<td>MCVI 94% MCV2 84%</td>
<td>14,176</td>
<td>640</td>
<td>2015/2015</td>
<td>Priorities</td>
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<tr>
<td>Western Pacific</td>
<td>MCVI 97% MCV2 93%</td>
<td>131,043</td>
<td>12,814</td>
<td>2012/2020*</td>
<td>China</td>
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<tr>
<td>Southeast Asia</td>
<td>MCVI 84% MCV2 59%</td>
<td>28,403</td>
<td>9,263</td>
<td>2020/TBD</td>
<td>India, Indonesia</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>MCVI 77% MCV2 66%</td>
<td>18,129</td>
<td>2,945</td>
<td>2015/TBD</td>
<td>Insecurity</td>
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<tr>
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<td>MCVI 73% MCV2 11%</td>
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<td>Weak health systems</td>
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<tr>
<td>Global</td>
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<td>267,482</td>
<td>33,068</td>
<td>TBD/TBD</td>
<td>Political will</td>
</tr>
</tbody>
</table>

*2020 target date approved in June 2015 by the Regional Technical Advisory Group, regional committee endorsement pending*