



Summary of the Thirtieth Meeting of the International Task Force for Disease Eradication (ITFDE) October 22, 2019

The 30th Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center in Atlanta, GA, USA from 8:30 am to 5:00 pm on October 22, 2019 to discuss the potential for eradication of measles and rubella. The Task Force members are Dr. Stephen Blount, The Carter Center (Chair); Dr. Peter Figueroa, The University of the West Indies, Jamaica; Dr. Donald Hopkins, The Carter Center; Dr. Fernando Lavadenz, The World Bank; Dr. Mwelecele Malecela, World Health Organization (WHO); Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Ana Morice, Independent Consultant; Dr. Stefan Peterson, UNICEF; Dr. David Ross, The Task Force for Global Health; Dr. William Schluter, Centers for Disease Control and Prevention (CDC); Dr. Nilanthi de Silva, University of Kelaniya, Sri Lanka/WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases (STAG-NTDs); Dr. Dean Sienko, The Carter Center; Dr. Laurence Slutsker, PATH; Dr. Jordan Tappero, Bill & Melinda Gates Foundation; Dr. Ricardo Thompson, National Institute of Health (Mozambique); and Dr. Dyann Wirth, Harvard School of Public Health. Eleven Task Force members (Blount, Figueroa, Hopkins, Morice, Ross, Sienko, de Silva, Slutsker, Tappero, Thompson, Wirth) participated in this meeting; three were represented by an alternate (Drs. Fatima Barry for Lavadenz, Steve Cochi for Schluter, Yodit Sahlemariam for Peterson). Presenters included Drs. Sunil Bahl, WHO/SEARO; Amanda Cohn, CDC; Matthew Hanson, Bill & Melinda Gates Foundation; Alan Hinman, The Task Force for Global Health; Mark Jit, London School of Tropical Medicine & Hygiene; Ann Lindstrand, WHO/Geneva; Balcha Masresha, WHO/AFRO; Patrick O'Connor, WHO/Europe; and Desiree Pastor, Pan American Health Organization (WHO/PAHO).

Introduction

The ITFDE previously considered the topic of measles and rubella eradication in 2015, when it reaffirmed its 2009 conclusion: “[we] firmly believe that both measles and rubella eradication are technically feasible, ...but a paradigm shift will be needed. ...Eradication will require a much more demanding enterprise than the current effort, which has suffered from insufficient resources and wavering political commitment.”¹ The ITFDE also concluded that “The impending completion of polio eradication opens a window of opportunity to devote greater attention to measles and rubella eradication.” The ITFDE reviewed the current status of global and regional elimination of measles and rubella at this meeting, with emphasis on the potential advantages of pursuing measles and

¹ Meeting of the International Task Force for Disease Eradication, November 2015. *Wkly Epidemiol Rec* 91(6): 61–71.

rubella eradication simultaneously, and the constraints of insufficient resources and political commitment.

Current Status

Measles remains a major cause of child mortality, and rubella is the leading cause of birth defects among all infectious diseases globally, even though both are vaccine-preventable.^{2,3,4} In 2010, an expert advisory panel convened by the World Health Organization (WHO) concluded that measles can and should be eradicated.⁵ The WHO Strategic Advisory Group of Experts (SAGE) on Immunization endorsed these conclusions, and in 2011, WHO's Executive Board endorsed the SAGE recommendations. In 2012, the WHA endorsed the Global Vaccine Action Plan (GVAP) that includes targets to achieve existing disease eradication and elimination goals for polio, neonatal tetanus, measles, and rubella by 2020. To enable decision-makers considering competing health priorities, GVAP emphasized that expenditures must be linked to outputs and impacts, showing the clear investment case for immunization goals.⁶ The new GVAP, the Immunization Agenda 2030, currently being developed, identifies measles as the tracer of inadequate immunization coverage and gaps in the health system and measles outbreaks highlights failure to reach every community with immunization services and emphasize therefore the continued efforts for every country and every WHO Region to reach elimination.

Following sustained investments in immunizations and surveillance, rubella (2015) and measles (2016) elimination were achieved and verified in the Region of the Americas. In the United States (US), elimination of endemic measles occurred in 2000 and of endemic rubella and CRS in 2004.^{7,8} The post-elimination era in the Americas has been characterized by ongoing measles virus importations from other regions, leading to costly outbreaks of varying size and duration.^{9,10}

² Vynnycky E, Adams E, Cutts F, Reef S, Navar A, Simons E, et al. Using Seroprevalence and Immunisation Coverage Data to Estimate the Global Burden of Congenital Rubella Syndrome, 1996-2010: A Systematic Review. *PLoS One*. 2016;11(3):e0149160-e.

³ Grant G, Reef S, Patel M, Knapp J, Dabbagh A. Progress in Rubella and Congenital Rubella Syndrome Control and Elimination - Worldwide, 2000-2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(45):1256-60.

⁴ Dabbagh A, Laws R, Steulet C, Dumolard L, Mulders M, Kretsinger K, et al. Progress Toward Regional Measles Elimination - Worldwide, 2000-2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(47):1323-9.

⁵ Strebel PM, Cochi SL, Hoekstra E, Rota PA, Featherstone D, Bellini WJ, et al. A World Without Measles. *J Infect Dis*. 2011 July 1, 2011;204(suppl 1):S1-S3.

⁶ Thompson K, Strebel P, Dabbagh A, Cherian T, Cochi S. Enabling implementation of the Global Vaccine Action Plan: developing investment cases to achieve targets for measles and rubella prevention. *Vaccine*. 2013;31 Suppl 2:B149-B56.

⁷ Papania MJ, Orenstein WA. Defining and assessing measles elimination goals. *J Infect Dis*. 2004 May 1;189 Suppl 1:S23-6.

⁸ Papania M, Wallace G, Rota P, Icenogle J, Fiebelkorn A, Armstrong G, et al. Elimination of endemic measles, rubella, and congenital rubella syndrome from the Western hemisphere: the US experience. *JAMA Pediatr*. 2014;168(2):148-55.

⁹ Fiebelkorn A, Redd S, Gastañaduy P, Clemmons N, Rota P, Rota J, et al. A Comparison of Postelimination Measles Epidemiology in the United States, 2009-2014 Versus 2001-2008. *J Pediatric Infect Dis Soc*. 2017;6(1):40-8.

¹⁰ Ortega Sanchez I, Vijayaraghavan M, Barskey A, Wallace G. The economic burden of sixteen measles outbreaks on United States public health departments in 2011. *Vaccine*. 2014;32(11):1311-7.

Experience in the Americas has shown that the strategic use of disease surveillance and vaccination¹¹ can lead to measles and rubella elimination; but, until eradication is achieved globally, outbreaks due to importations will persist.^{12,13} A large measles outbreak in Venezuela in 2018 spread to other countries in South America, leading to re-establishment of endemic transmission in Venezuela and Brazil, and loss of regional measles elimination verification status in the Americas, although the region remains verified for rubella elimination. Measles outbreaks have also occurred in all other WHO regions in 2018 and 2019.

Despite success in the Americas, in 2016 a Mid-Term Review (MTR) of the Global Measles and Rubella Strategic Plan 2012–2020 stated that failure to achieve any of the 2015 global mid-term goals and milestones indicated it was premature to set a measles and rubella eradication goal at that time.¹⁴ The MTR concluded that the basic strategic approaches articulated in the plan remained valid, but had not been fully implemented, largely due to lack of global political will reflected in inadequate resources and in some cases, a lack of country ownership.^{5,15} To build country commitment, SAGE recommended establishment of national verification committees and regional verification commissions to validate review evidence of progress towards and achievement of measles and rubella elimination. The MTR noted that a comprehensive evaluation should be undertaken no later than 2020, to determine an eradication goal timeframe.¹³

Some key donors have expressed reservations about committing resources to achieve the GVAP goals for measles and rubella elimination. The average annual funding during 2001–2016 was US\$69 million for the Measles and Rubella Initiative, in contrast to US\$818 million for the Global Polio Eradication Initiative. As polio eradication nears, transitioning polio assets, infrastructure, and lessons learned to measles and rubella elimination would maximize returns on donor and country investments.^{1,13,16} In the absence of a formal measles and rubella eradication goal, the

¹¹ Castillo-Solorzano C, Marsigli M, Bravo-Alcantara P, Flannery B, Ruiz Matus C, Tambini G, Gross-Galiano S, Andrus JK. Elimination of Rubella and Congenital Rubella Syndrome in the Americas. *J Infect Dis* 2011; 204:S571-S578.

¹² Orenstein W, Seib K. Mounting a good offense against measles. *N Engl J Med*. 2014;371(18):1661-3.

¹³ Goodson J, Seward J. Measles 50 Years After Use of Measles Vaccine. *Infect Dis Clin North Am*. 2015;29(4):725-43.

¹⁴ Orenstein WA, Hinman A, Nkowane B, Olive JM, Reingold A. Measles and Rubella Global Strategic Plan 2012-2020 Midterm Review; 2016. http://www.who.int/immunization/sage/meetings/2016/october/1_MTR_Report_Final_Color_Sept_20_v2.pdf?ua=1. 2016.

¹⁵ World Health Organization. Global Measles and Rubella Strategic Plan 2012-2020. 2012. http://www.who.int/immunization/newsroom/Measles_Rubella_StrategicPlan_2012_2020.pdf (accessed March 7, 2013).

¹⁶ Goodson JL, Alexander JP, Linkins RW, Orenstein WA. Measles and rubella elimination: learning from polio eradication and moving forward with a diagonal approach. *Expert Rev Vaccines*. 2017 2017/12/02;16(12):1203-16.

current approach of maintaining high control, currently costing governments and donors US\$2.3 billion per year, will continue.^{2,17,18,19,20}

The economic benefits of investing in vaccines, particularly measles-rubella vaccines, are well established.^{21,22,23,24} Broadly, vaccines have an estimated overall 44-fold return on investment (uncertainty range: 27–67);²⁰ the highest return on investment is for the measles vaccine (58-fold uncertainty range: 28–105) after provision of two routine immunization doses and outreach campaigns.²¹

The feasibility and benefits of measles and rubella eradication are well established.^{23,25,26,27,28} Eradication of both diseases can be done together. Inexpensive, highly effective combined measles and rubella vaccines can be administered, and both diseases can be detected through rash-fever case-based surveillance.²⁹ The basic reproductive number (R_0) for rubella is 6–7 and for measles is 12–18; with corresponding calculated herd immunity thresholds of 83%–85% for rubella and 92%–94% for measles. Herd immunity thresholds can be reached with one dose of vaccine for rubella and two doses for measles. Therefore, the biggest technical challenge in a combined eradication effort is the high transmissibility of measles virus.^{16,28,30,31}

¹⁷ Patel M, Gacic Dobo M, Strebel P, Dabagh A, Mulders M, Okwo Bele J-M, et al. Progress Toward Regional Measles Elimination - Worldwide, 2000-2015. *MMWR Morb Mortal Wkly Rep.* 2016;65(44):1228-33.

¹⁸ Thompson K, Odahowski C. The Costs and Valuation of Health Impacts of Measles and Rubella Risk Management Policies. *Risk Analysis.* 2016;36(7):1357-82.

¹⁹ Thompson KM, Odahowski CL, Goodson JL, Reef SE, Perry RT. Synthesis of Evidence to Characterize National Measles and Rubella Exposure and Immunization Histories. *Risk Analysis.* 2016;36(7):1427-58.

²⁰ Thompson KM, Strebel PM, Dabagh A, Cherian T, Cochi SL. Enabling implementation of the Global Vaccine Action Plan: developing investment cases to achieve targets for measles and rubella prevention. *Vaccine.* 2013 Apr 18;31 Suppl 2:B149-56.

²¹ Ozawa S, Clark S, Portnoy A, Grewal S, Brenzel L, Walker D. Return On Investment From Childhood Immunization In Low- And Middle-Income Countries, 2011-20. *Health Affairs.* 2016;35(2):199-207.

²² Lee LA, Franzel L, Atwell J, Datta SD, Friberg IK, Goldie SJ, et al. The estimated mortality impact of vaccinations forecast to be administered during 2011-2020 in 73 countries supported by the GAVI Alliance. *Vaccine.* 2013 Apr 18;31 Suppl 2:B61-72.

²³ Ozawa S, Clark S, Portnoy A, Grewal S, Stack M, Sinha A, et al. Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001-2020. *World Health Organization Bulletin of the World Health Organization.* 2017;95(9):629-38.

²⁴ Thompson K, Badizadegan N. Modeling the Transmission of Measles and Rubella to Support Global Management Policy Analyses and Eradication Investment Cases. *Risk Analysis.* 2017;37(6):1109-31.

²⁵ Robbins FC. Prospects for Worldwide Control of Measles: Discussion I. *Rev Infect Dis.* 1983;5(3):619-20.

²⁶ Dowdle W, Cochi S. The principles and feasibility of disease eradication. *Vaccine.* 2011;29 Suppl 4:D70-3.

²⁷ CDC. Recommendations of the International Task Force for Disease Eradication. *Morbidity and Mortality Weekly Report* 1993; 42(RR-16):8.

²⁸ Peter M, Strebel MJP, Paul A, Gastañaduy, and James L. Goodson. Measles Vaccines. In: Stanley Plotkin WO, Paul Offit, Kathryn M. Edwards, editor. *Vaccines* (Seventh Edition) 7th ed. Philadelphia, PA: Elsevier; 2018. p. 579-618.

²⁹ Cochi S. Pivoting from polio eradication to measles and rubella elimination: a transition that makes sense both for children and immunization program improvement. *Pan Afr Med J.* 2017;27(Suppl 3):10-.

³⁰ Rota P, Moss W, Takeda M, de Swart R, Thompson K, Goodson J. Measles. *Nat Rev Dis Primers.* 2016;2:16049-.

³¹ Kretsinger K, Strebel P, Kezaala R, Goodson JL. Transitioning Lessons Learned and Assets of the Global Polio Eradication Initiative to Global and Regional Measles and Rubella Elimination. *J Infect Dis.* 2017;216(suppl_1):S308-S15.

At the end of 2019, only 21 countries (18 of which are Gavi-eligible) still need to introduce rubella-containing vaccine (RCV). Gavi received \$500 million in 2012 donations to complete RCV introduction in Gavi-eligible countries. Completion of this objective should be a priority over the next 2-3 years to prepare for rubella eradication. Routine use in children of measles- and rubella-containing vaccine (MR vaccine) should become the standard of care worldwide within the next 3 years.

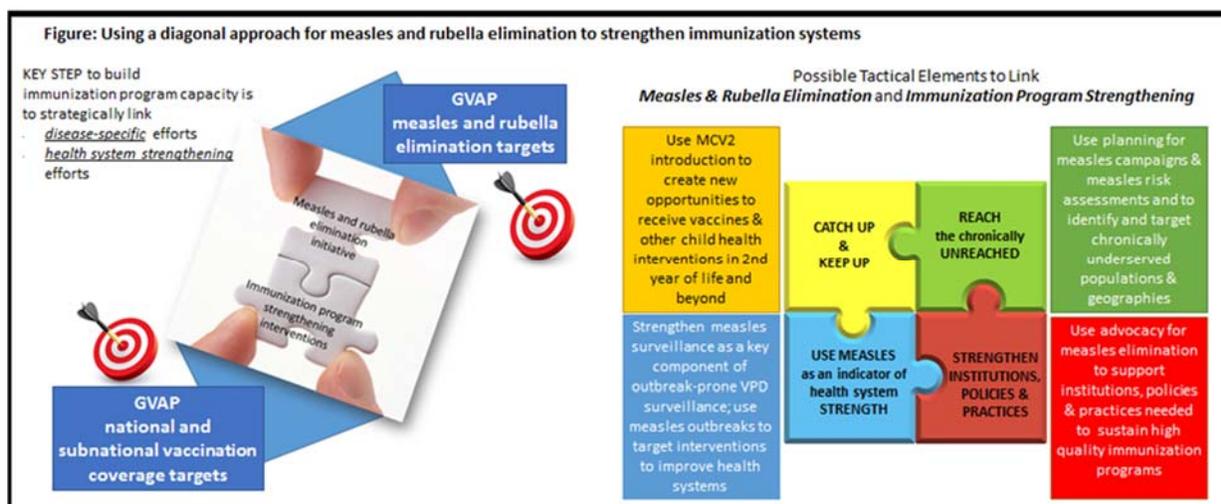
Incomplete reach of immunization programs in some low and middle-income countries has led to susceptibility gaps in cohorts of older children and/or young adults, making the prospect of measles and rubella eradication increasingly difficult and costly over time.

Strengthening routine immunization services in low performing countries is a requirement for achieving measles and rubella eradication. A lesson learned from polio eradication is the need to closely link measles-rubella activities with overall improvement of immunization program performance. Several tactical approaches, collectively called “the diagonal approach,” can be used to link strategies for measles-rubella eradication with strategies to strengthen immunization programs.^{28,30,32}

The Diagonal approach: The approach taken is to move beyond the stereotypical vertical vs. horizontal approach to implementing health initiatives. This third way focuses on building national immunization programs and on achieving targeted disease objectives simultaneously, as recently described by Orenstein.³² Measles is particularly amenable to this approach and its contagiousness makes it clear that close attention to both aspects of the “diagonal” construct is required for successful eradication. Four tactics are summarized in the recommendations below, are proposed to link measles and rubella eradication efforts with strengthening immunization programs to reach their respective GVAP goals (Figure):

1. Catch-up and keep up – Use MCV2/MRCV2 introduction to create new opportunities to receive vaccines and other child health interventions in the second year of life and beyond.
2. Use measles as an indicator of health system strength – Improve measles surveillance as a key component of outbreak-prone VPD surveillance and use measles outbreaks to target interventions for improving health systems.
3. Reach the chronically unreached – Use planning for measles campaigns and measles risk assessments to identify and target chronically underserved populations and geographies.
4. Strengthen institutions, policies and practices – Use advocacy for measles and rubella eradication to support institutions, policies and practices needed to sustain high quality immunization programs.

³² Orenstein W, Seib K. Beyond vertical and horizontal programs: a diagonal approach to building national immunization programs through measles elimination. *Expert Rev Vaccines*. 2016;15(7):791-3.



Conclusions and Recommendations

1. Measles vaccination is estimated to have prevented 21.1 million deaths globally from 2000-2017,⁴ but measles remains an important and preventable cause of child morbidity and mortality, including an estimated annual burden of over 100,00 deaths. The return on investment afforded by measles vaccine surpasses that of any other vaccine, with an estimated \$58 saved in future costs for every \$1 spent.^{19,21}
2. Rubella is the leading infectious cause of congenital birth defects. Remarkable progress has been achieved in introducing rubella 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 congenital rubella syndrome (CRS). However, approximately 105,000 infants are born each year with preventable CRS.² Rubella vaccine use in routine childhood immunization schedules has increased from 99 (51%) countries in 2000 to 168 (87%) countries as of July 2019, and the Region of the Americas has interrupted endemic rubella transmission since 2009.
3. Despite measles outbreaks in all WHO regions, and with global incidence increased from 18 reported cases / million population in 2016 to 50 reported cases/ million in 2018, the ITFDE continues to believe firmly that both measles and rubella eradication are technically feasible, and that both should be eradicated. The ITFDE believes more can and should be done by global health and donor organizations to adequately support efforts by WHO regions and countries, all of which by 2013 had committed to regional measles elimination targets.
4. The economic literature and the measles-rubella investment case confirm that measles-rubella eradication is more cost effective than indefinite control and the ITFDE strongly encourages all partners to make this case to decision-makers as often as possible.
5. As noted at the 2015 ITFDE meeting, the impending completion of polio eradication opens a window of opportunity to improving efforts to integrate/link GPEI with measles and rubella eradication and its essential requirement for a strong immunization program platform. Increased country and regional efforts against the continued high burden of measles and rubella/CRS must occur in a manner that does not jeopardize achievement of polio eradication.

6. A lesson learned from polio eradication is the need to closely link measles-rubella activities with improvement of immunization programs and national health systems performance. Because measles is so infectious, each village/ settlement must provide immunizations regularly; periodic campaigns are not timely enough. The call for universal health care aligns with efforts of wealthy countries, donor organizations and others to achieve global health security, since most new measles cases in the US and Europe are imported. Using the **Diagonal approach described in the body of the report**, four tactics for linking measles-rubella eradication with routine immunization and health system strengthening should be pursued, as described above.
7. Despite such challenges as increased population density, conflict, and decreased funding, efforts to reach measles and rubella eradication should be re-doubled. The ITFDE is aware that establishment of a target date for measles eradication at this time remains controversial, but the resurgence of measles since 2018 demonstrates the risks and consequences of a lack of a firm commitment to eradication.
8. A target date for rubella eradication should be established, perhaps 2030, regardless of whether a measles eradication target date is set, since most experts agree rubella will be easier to eradicate than measles. Universal childhood immunization against rubella is rapidly approaching, rubella incidence is declining worldwide, and rubella is far less contagious than measles. The ITFDE believes rubella eradication is achievable within the next decade. Universal routine vaccination of children with MR-containing vaccine should become the standard of care worldwide within the next 3 years. The ITFDE encourages discussion of the feasibility and potential timing of such a global commitment at the next World Health Assembly in 2020.
9. To stop measles outbreaks in many countries and improve global health security, the ITFDE supports establishing measles immunization requirements for international travel, both for citizens traveling outside their home countries and visitors entering countries.
10. In the face of the growing hesitancy by some parents and some communities to immunize their children, the ITFDE notes the important work of public and private allies to better understand and counteract this hesitancy. This requires a cohesive strategy linking national and local governments in every country, as well as key stakeholders and providers, to protect communities, educate families and stop myths.
11. In 2015, the ITFDE declared, “The thermostable microneedle patch for delivery of measles and rubella vaccine seems especially promising and innovative but urgently needs funding for clinical testing.” Despite the promise that it could be a ‘game changer,’ development has proceeded very slowly due to inadequate funding. The ITFDE strongly recommends that greater investments be made to bring this innovation into public health practice.