

**Verification and Documentation of Elimination of Measles and Rubella as
Endemic Diseases from the United States:
Summary and Conclusions of an External Expert Panel**

Expert Panel

Alan R. Hinman, MD, MPH (Chair)¹, Christine Hahn, MD², Yvonne Maldonado, MD³,
Peter A. Shult, PhD⁴, Jonathan L. Temte, MD, MS, PhD⁵

Each of the Panelists supports the content and conclusions of this report.

Rapporteur

Susan E. Reef, MD⁶

Dr. Reef served as the Rapporteur for the Panel and in that capacity, drafted this Report for review and finalization by expert panel members.

¹ Task Force for Global Health, Decatur GA

² Idaho Department of Health and Welfare, Boise ID

³ Department of Pediatrics, Division of Infectious Diseases, Stanford University School of Medicine, Stanford, CA

⁴ Communicable Disease Division and Emergency Laboratory Response, Wisconsin State Laboratory of Hygiene, Madison WI

⁵ Department of Family Medicine, University of Wisconsin School of Medicine and Public Health, Madison WI

⁶ Global Immunization Division, Center for Global Health, Centers for Disease Control and Prevention, Atlanta GA

Introduction

On December 16, 2011, the Division for Viral Diseases (DVD), National Center for Immunizations and Respiratory Diseases (NCIRD), Centers for Disease Control and Prevention (CDC) convened 5 consultants to review the present status of sustained elimination of endemic measles, rubella and congenital rubella syndrome (CRS) in the United States and to provide individual opinions on 3 questions:

1. Is the evidence presented in the draft national report sufficient to document the sustained elimination of endemic measles from the United States?
2. Is the evidence presented in the draft national report sufficient to document the sustained elimination of endemic rubella and CRS from the United States?
3. If the evidence presented is not sufficient to make such conclusions, what additional information is required?

The United States had previously verified the elimination of endemic measles in 2000 (J Infect Dis. 2004 May 1;189 Suppl 1) and of rubella and CRS in 2004 (Clin Infect Dis. 2006 Nov 1;43 Suppl 3.). In accordance with the PAHO mandate of 2007 (<http://www.paho.org/english/gov/csp/csp27.r2-e.pdf>) the United States is undergoing re-verification of endemic measles, rubella and CRS and CDC prepared a draft national report that was the basis for discussions at the meeting.

A brief description of the PAHO process for documentation of elimination of measles, rubella, and CRS was provided to the panel. Each country and the countries in the Caribbean as a subregion were asked to conduct a national review. In October 2007, a resolution requested Member States to begin the process of documentation and verification of the interruption of endemic measles and rubella virus transmission in the Americas. In December 2010, the International Expert Committee (IEC) was established. On December 12, 2011, IEC was updated on the progress toward the documentation.

Epidemiology of measles, rubella, and CRS

In 2000, measles elimination was documented and verified in the United States. During 2001-2011, a total of 904 cases (range: 37-212/year) was reported, with median annual incidence of 60 cases. In 2011, 212 measles cases were reported⁷, the highest number since 1996; however, the incidence has remained less than 1/ million population continuously since 1997. The highest incidence in recent years occurred in 2008 and 2011. The highest age-specific incidence rate was among infants too young to be vaccinated. The majority of the measles cases (2001-2011) were unvaccinated (65%) or had unknown vaccination status (20%). A majority (88%) of the cases represented importations or import-associated infections. Although there was an

⁷ 212 is the provisional total for measles cases reported to CDC and is used for data summarized throughout the report. The total number of measles cases reported to CDC by December 31st 2011 (222) is mentioned in the challenges section of the report.

increase in importations in 2011, spread from these importations was limited. In comparing the R_0 (effective reproduction number) between 1997-1999 and 2002-2011, the R_0 was 0.63 and 0.7, respectively, and was in both time periods below the elimination value threshold of 1.0. During 2001-2011, 64 outbreaks were reported. The median size of the outbreaks was 6 cases with the largest having 34 cases. The longest outbreak lasted 11 weeks. During 2001-2011, 12 different genotypes were identified with 3-6 different genotypes identified each year.

Rubella and CRS elimination was documented and verified in the United States in 2004. During 2005-2011, a median of 10 rubella cases/year was reported. During that period, 4 cases of CRS were reported. Incidence of rubella was less than 1 per 10 million and incidence of CRS was less than 1 per 5 million births. There were 2 rubella outbreaks, each with 3 cases. Approximately 39% of rubella cases and 3 of the 4 CRS cases were known to represent importations. From 2008-2011, 12 viruses representing 4 different genotypes were identified among the 34 laboratory-confirmed rubella and CRS cases.

Review of the Draft National Report

After a review of the definitions and processes for surveillance and investigation, discussions turned to a review of the information on the epidemiology of measles (2001-2011) and the epidemiology of rubella and CRS (2004-2011); followed by considerations of the quality of surveillance and outbreak response; assessment of measles and rubella population immunity; sustainability of measles, rubella and CRS elimination; correlation and integration of the evidence for maintenance of elimination of measles, rubella, and CRS; and challenges. The important issues that will require ongoing discussion and actions from the US measles, rubella and CRS program are summarized below.

1) Classification of cases

In reviewing measles and rubella laboratory surveillance activities, it was noted that private laboratories provide a majority of the initial testing. Currently there are 4-5 large commercial laboratories. The accuracy of the results from the commercial laboratory is not known with certainty. In addition, the volume of testing performed by the commercial and clinical laboratories is unknown. All state health department laboratories have the capacity to perform testing or have access to testing. In addition, some state laboratories have been developed as Reference Centers to provide increased capability and surge capacity for vaccine-preventable disease testing.

With the interruption of endemic measles and rubella, and low number of cases, it is anticipated that there will be false IgM positives. In addition to the low positive predictive value (PPV) with decreasing incidence of disease, there is variability in serological testing among laboratories, both public and commercial. The panel discussed the need for confirmatory testing to accurately classify the cases. Given

the questions concerning quality and capacity for measles and rubella testing, it was felt that the Reference Centers should continue to increase their capability and capacity for performing confirmatory testing for measles and rubella.

2) Methods for Surveillance and outbreak investigation and response:

The surveillance systems for measles, rubella and CRS are passive; however, there is active investigation of suspected cases. The committee felt that this was an important distinction. The detection of cases is predicated on the ongoing suspicion of cases. In a low incidence setting, clinicians are less likely to suspect measles and rubella. Reporting of suspected cases is mandatory in all states. However, reporting is dependent on many factors including identification of suspected cases, reporting of cases to health departments and investigation of cases. There is currently no nationwide metric or standard approach for completeness of reporting.

Discussion centered around the adequacy of surveillance. In documenting the interruption of measles in 2000, a comprehensive evaluation of the adequacy of surveillance was conducted; however, no comprehensive assessment has been conducted since then. To assess adequacy, some suggestions included monitoring the discard rate of suspected cases and conducting an assessment of laboratory confirmed cases not reported; however, that may not include private laboratories. Monitoring the number of suspected cases that were discarded is currently used by most of the countries in the region of Americas. As part of the assessment in 2000, it was felt that a system of reporting of suspected and discarded cases couldn't be maintained in the US and wasn't worth implementing in the US. It was felt that there were other measures (e.g., detection of imported and isolated cases) to assess the adequacy of surveillance.

When discussing the adequacy of surveillance, it was felt that even though some cases may be missed, these do not represent large numbers of missed cases or outbreaks. If many cases were missed, larger numbers of outbreaks would be detected, especially outbreaks with unidentified index cases or for whom no sources of infection for index cases could be identified, as well as detection of additional previously un-reported cases on investigation of these outbreaks. In the past several years, the index case has generally been identified with secondary cases identified. After review of the data, panel members felt that, while isolated cases were likely being missed, large outbreaks were not.

To continue to maintain adequate surveillance, it is important to maintain awareness of measles, rubella and CRS through education about the diseases. The US program continues to publish MMWR and journal articles to increase awareness of the diseases both for the public and for health care providers. Concern still was expressed that healthcare workers are not well trained in diagnosis of measles, rubella and CRS because of the rarity of the conditions. Additional emphasis will be

needed to continue to maintain the awareness of diseases, including preparation of pictures of patients of different races/ethnicities.

3) Epidemiology of measles

Understanding the temporal and geographical distribution of cases is critical. Several outbreaks and cases were close to state lines. For cases with known or unknown genotypes, there needs to be clarity of whether there was transmission across state lines which may be related to endemic transmission. In addition, R_0 as calculated for the pre-elimination period should be calculated for the post-elimination period (this has been done).

Conclusions and Recommendations:

The data indicate that existing surveillance systems are adequate to detect endemic measles, rubella, and CRS. Elimination has been maintained in the United States, despite challenges that include ongoing risk of importations, healthcare worker lack of familiarity with these diseases, maintaining a continued high level of public health response, and through maintaining high 2-dose coverage.

Even though elimination has been maintained, several recommendations were made:

- Raise and sustain awareness among healthcare workers of the continuing possibility of vaccine-preventable diseases, including training of residents in communicating with patients and parents
- Need to consider methods and metrics to monitor completeness of reporting
- Increased emphasis should be given to US travelers to ensure that they are adequately protected against measles and rubella, regardless of age. This should include education of providers and travelers
- The US needs to be involved globally and domestically to protect its citizens, reduce death and disease overseas, reduce importations and reduce the costs of controlling diseases.
- Update photographs and visual media on measles and rubella in persons of different ethnicities.
- Try to incorporate algorithms into electronic medical record systems to enhance completeness of diagnosis and reporting

Vaccine refusals

- The level of vaccine reluctance and refusal is of concern. If it continues to rise, it will pose a threat to sustainability of measles and rubella/CRS elimination. Both public and private sectors need to be engaged to reduce the level of vaccine refusals both domestically and globally.
- Clinicians need appropriate tools for communicating vaccine safety. Some materials have recently been developed.

Laboratory issues

- Routine collection of the number of IgM tests for measles and rubella performed would help to buttress the evidence for sustained elimination
- Evaluate the use of electronic laboratory records to monitor the volume of testing for measles and rubella
- Ensure capability and capacity of testing for measles and rubella is maintained at public health laboratories

Rubella/Measles

- Work with CSTE to refine case definitions including laboratory confirmation

In answer to the three questions initially posed to the panel, each member of the panel concluded that **elimination has been achieved and maintained. However, elimination is inherently a fragile state. As long as there are continued importations, a significant level of surveillance, investigation, and response will be needed to sustain elimination.**