

cision and comparability of results from surveillance, epidemiological studies, and biological investigations. Studies should also address the heterogeneity in the etiology of ASD and the spectrum of clinical presentation.

The committee reaffirms its previous recommendation to conduct clinical and epidemiological studies of sufficient rigor to identify risk factors and biological markers of ASD in order to better understand genetic or environmental causes of ASD.

Surveillance of adverse events related to vaccines is important and should be strengthened in several ways:

The committee recommends that standardized case definitions for adverse events be adopted.

The committee recommends that formal guidelines or criteria be developed for using VAERS data to study adverse events.

The committee recommends the continued use of large-linked databases, active surveillance, and other tools to evaluate potential vaccine-related adverse events.

The committee supports the development of Clinical Immunization Safety Assessment (CISA) centers to improve understanding of adverse events at the individual level.

One area of complementary research that the committee continues to recommend is surveillance of ASD as exposure to thimerosal declines.

The committee recommends increased efforts to quantify the level of prenatal and postnatal exposure to thimerosal and other forms of mercury in infants, children, and pregnant women.

#### *Clinical Studies*

Because chelation therapy has potentially serious risks, the committee recommends that it be used only in carefully-controlled research settings with appropriate oversight by Institutional Review Boards protecting the interests of the children who participate.

#### *Communication*

Better risk-benefit communication requires attention to the needs of both the scientific community and public communities. Many scientists need to develop a more comprehensive understanding of what risk-benefit communication entails and the rich knowledge base that can be used to design strategic communication programs. Thus, the committee recommends developing programs to increase public participation in vaccine safety research and policy decisions and to enhance the skills and willingness of scientists and government officials to engage in constructive dialogue with the public about research findings and their implications for policy development.

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# IMMUNIZATION SAFETY REVIEW

## VACCINES AND AUTISM

Immunization Safety Review Committee  
Board on Health Promotion and Disease Prevention

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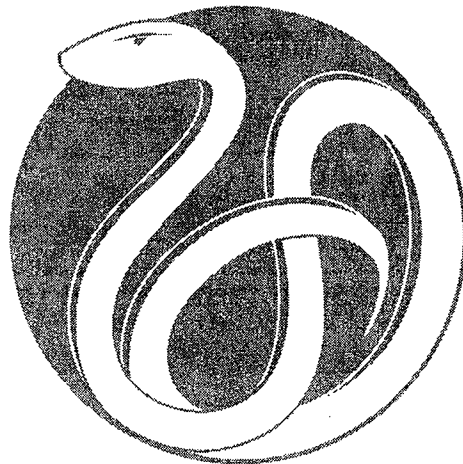
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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

*“Knowing is not enough; we must apply.  
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## Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

**Ann Bostrom**, Georgia Institute of Technology  
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**Andrew Zimmerman**, Johns Hopkins University

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Robert S. Lawrence**, Johns Hopkins University, and **Floyd E. Bloom**, Scripps Research Institute. Appointed by the National Research Council and Institute of Medicine, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

## Foreword

Vaccines are among the greatest public health accomplishments of the past century. In recent years, however, a number of concerns have been raised about both the safety of and the need for certain immunizations. Indeed, immunization safety is a contentious area of public health policy, with discourse around it having become increasingly polarized and exceedingly difficult. The numerous controversies and allegations surrounding immunization safety signify an erosion of public trust in those responsible for vaccine research, development, licensure, scheduling, and policymaking. Because vaccines are so widely used—and because state laws require that children be vaccinated to enter daycare and school, in part to protect others—immunization safety concerns should be vigorously pursued in order to restore this trust.

It is in this context that the Institute of Medicine (IOM) was approached over three years ago by the Centers for Disease Control and Prevention and the National Institutes of Health to convene an independent committee that could provide timely and objective assistance to the Department of Health and Human Services in reviewing emerging immunization safety concerns.

The IOM was chartered by the National Academy of Sciences in 1970 to serve as an adviser to the federal government on issues affecting the public's health, as well as to act independently in identifying important issues of medical care, research, and education. The IOM thus brings to this mission three decades of experience in conducting independent analyses of significant public health policy issues. In particular, as described in more detail in this report, the IOM has a long history of involvement in vaccine safety. The IOM published its first major vaccine safety report in 1977, followed by a subsequent report in 1988; both

focused on the safety of polio vaccines. Two subsequent major reports, published in 1991 and 1994, examined the adverse effects of childhood vaccines. Since then, the IOM has conducted several smaller studies and workshops focused on various vaccine safety topics. These studies were well received by both the public and policymakers, and previous IOM committees on vaccine safety issues have been viewed as objective and credible.

Given the sensitive nature of the present immunization safety review study, the IOM felt it was especially critical to establish strict criteria for committee membership. These criteria prevented participation by anyone with financial ties to vaccine manufacturers or their parent companies, or who had given expert testimony on issues of vaccine safety.

The rationale for imposing these stringent criteria was twofold. First, given growing public concern about vaccine safety and the public scrutiny surrounding this committee's work, it was important to establish standards that would preclude any real or perceived conflict of interest or bias on the part of the committee members. No member has any vested interest in any of the vaccine safety questions that will come before the committee. Second, the IOM wanted to ensure that no committee member had participated in the development or evaluation of a vaccine under study.

Thus, the IOM has convened a distinguished panel of 13 members who are experts in a number of pertinent fields, including pediatrics, neurology, immunology, internal medicine, infectious diseases, genetics, epidemiology, biostatistics, risk perception and communication, decision analysis, public health, nursing, and ethics. The committee members were chosen because they are leading authorities in their respective fields, are well respected by their colleagues, and have no conflicts of interest. This committee brought a fresh perspective to these critically important issues and approached its charge with impartiality and scientific rigor.

As with all reports from the IOM, the committee's work was reviewed by an independent panel of experts. The purpose of the review process is to enhance the clarity, cogency, and accuracy of the final report and to ensure that the authors and the IOM are creditably represented by the report published in their names. The report review process is overseen by the National Research Council's (NRC) Report Review Committee (RRC), comprising approximately 30 members of the National Academy of Sciences, National Academy of Engineering, and IOM. A select panel of reviewers with a diverse set of perspectives are asked to critique the report. Unlike the selection criteria for committee membership, many reviewers will have strong opinions and interests related to the report topic. The composition of the review panel is not disclosed to the committee until after the report is approved for release. While the committee must consider and evaluate all comments from reviewers, it is not obligated to change its report in response to the reviewers' comments. The committee must, however, justify its responses to the reviewers' comments to the satisfaction of the RRC's review monitor and the IOM's review coordinator. A report may not be released to the sponsors or the

*FOREWORD*

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public, nor may its findings be disclosed, until after the review process has been satisfactorily completed and all authors have approved the revised draft.

This report represents the unanimous conclusions and recommendations of that dedicated committee whose members deliberated a critical health issue. I am grateful to the committee and its able staff for their efforts on behalf of the public's health.

Harvey V. Fineberg  
President, Institute of Medicine

## Acknowledgments

The committee would like to acknowledge the many speakers and attendees at its open meeting held on February 9, 2004, at the National Academy of Sciences building in Washington, DC. The discussions were informative and helpful. The committee would also like to thank those people who submitted information to the committee through the mail or via e-mail. Finally, the committee thanks the IOM staff for their dedication to this project. Without their commitment, attention to detail, creativity, sensitivity, and hard work, this project would be unworkable.

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