



April 13, 2009

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Ellen Wright Clayton, J.D., M.D.

Chair, IOM Committee to Review Adverse Effects of Vaccines [via email to [vaccinesafety@nas.edu](mailto:vaccinesafety@nas.edu)]

**RE: Review of Adverse Effects of Vaccines, PPHH-H-08-17-A**

Dear Drs. Fineberg, Wakefield and Clayton, and Ms. Somsak:

HRSA announced in October 2008 that it had awarded a 2 year contract to the IOM to study adverse events associated with certain childhood vaccines. The first meeting of the Committee to Review Adverse Effects of Vaccines is scheduled for April 20. We have concerns over the manner in which IOM reviews on vaccine safety have been conducted in the past. Given the new Administration's emphasis on openness in government and a return to science, we ask the IOM to adjust its practices accordingly. For this review on adverse effects of vaccines, we wish to see complete transparency, provision for broader

public participation in all facets of the process, a balance of scientific views and expertise, and an absence of conflicts of interest on the committee.

The findings of this IOM study will likely have great impact on the thousands of families who have cases in the Vaccine Injury Compensation Program. The findings may be used by HRSA, in consultation with ACCV, to revise the vaccine injury compensation table. The scope of work given by HRSA to IOM is as follows:

Project scope: The committee will review the epidemiological, clinical, and biological evidence regarding adverse health events associated with specific vaccines covered by the Vaccine Injury Compensation Program. The vaccines to be reviewed are varicella zoster vaccine, influenza vaccines, hepatitis B vaccine, and human papillomavirus vaccine. Other vaccines could be added if additional funding is secured. The committee will author a consensus report with conclusions on the evidence bearing on causality and the evidence regarding the biological mechanisms that underlie specific theories for how a specific vaccine is related to a specific adverse event.

*Past deficiencies in the process*

IOM has assigned Kathleen Stratton to be the Responsible Staff Officer (RSO). Ms. Stratton's private closed-door statements during past vaccine safety review deliberations raise concerns about her objectivity and that of the IOM on the issue of vaccine adverse effects, in particular prejudging the evidence and the potential impact of the evidence on government policy before it is presented, and in steering discussions to a predetermined outcome.

The 2004 report on thimerosal and MMR association with autism ran counter to the scientific process. The report made a recommendation to no longer conduct any research on autism and vaccines and to redirect research funds to "other promising areas". Such a recommendation is tantamount to a policy of deliberate ignorance in an area - vaccine safety - that in fact requires "overinvestment" to protect public confidence.

The IOM 2004 report failed to meet the standards expected of IOM: it contained a woefully inadequate bibliography; it overly relied on deeply and objectively flawed epidemiology; it minimized the significance of bench science and challenge/rechallenge evidence; and its closed-door discussions were pre-occupied with "policy" implications rather than science.

Public input was minimized in past reviews. Consumer stakeholders were left in the dark about the framing of the questions to the committee, had no input on the committee membership, were not privy to any of the deliberations, and had no opportunity to comment on the report before it was finalized. The committee membership was extremely biased in favor of champions of the existing vaccine program and lacked expertise in several critical fields.

We do not want to see these past deficiencies repeated in the next round of vaccine safety reviews. We ask for the following changes.

1. Expand the scope of the review

How this review is conducted may have a noticeable impact on public confidence in vaccines. Confidence heavily depends on two factors converging within this review: (a) the existence of sound and adequate safety science leading to the safest possible vaccine schedule for each individual child and the identification of the likely adverse outcomes from vaccination, and (b) an effective "safety net" in the form of a vaccine court seen as applying sound and adequate science in a fair and consistent manner. The vaccine court off-table procedure is deeply dysfunctional. Over the past decade, the majority of court cases have become off-table. Continued confidence in immunizations requires a workable table consistent with the congressional mandate that scientific doubt be resolved in favor of families to protect the dual purposes of the VICA.

We feel that more vaccines should be added to the review. It is unclear how just four vaccines, out of the dozen or so regularly given to children, were selected as priorities. Moreover, an assessment of how vaccines *as a class* might lead to a range of similar adverse effects is needed. Examination of adverse outcomes from the childhood vaccine schedule as a whole, rather than individual vaccines, should also be considered.

2. Respond appropriately when evidence is inadequate

In the past, the IOM has agreed to requests to review the evidence when it was known that sufficient evidence did not exist to conduct an adequate review. Findings of insufficient evidence to determine causality or biological plausibility have several insidious effects: Vaccine Court Special Masters must then "guess" about the evidence in a particular case; families with an injured child may be advised against petitioning the court as their case will be seen as unwinnable; and physicians will not be aware that they should look for certain adverse outcomes after giving a vaccine.

The IOM should refuse to accept a request from HRSA to issue a finding on a question when the committee has found that inadequate evidence exists, especially when the government has failed to provide funding to conduct the research to produce the evidence. The committee should refuse to issue findings in such cases and rather insist that the government undertake the research.

The panel should be specifically tasked to identify gaps in the five evidence categories and make recommendations as to how they could be filled, as opposed to passively reacting to the current state of knowledge. The CDC spends only \$20 million annually on vaccine safety studies while allocating billions of dollars to vaccine promotion. The committee should above all strongly communicate to HHS the urgent need for an aggressive safety first agenda.

### 3. Modify the charge to the committee

IOM's reputation depends on both the appearance and reality of independence from government. HRSA has awarded IOM the contract and is providing the “charge to the committee”, meaning it gets to determine what questions are asked and what should be considered in answering them. The specifics of the charge has a deep impact on the outcome, as the committee can only answer the questions asked, is limited in the answers it can give, and can only examine evidence pertinent to the question. Although HRSA oversees the Vaccine Court, it is also the defendant in Vaccine Court. Thus it has an enormous conflict of interest in what the IOM committee finds. HRSA should not be the party determining the charge to the committee. To minimize bias, the questions to be answered for each of the vaccines examined should be open to public comment and revisions made based on these comments.

As a start, we ask that the standard of proof for causality be reinterpreted from needing to link a specific biological mechanism to a specific disorder or symptom. Rather, biological plausibility should be interpreted to mean the general principles of biological mechanisms through which an observed disorder or symptom may be produced by an intermediate effect, such as neuroinflammation or demyelination. Animal model and cell culture data, from which human disease outcomes are difficult to interpret, should be utilized for this assessment.

### 4. Ensure diversity in committee membership and eliminate conflicts of interest

We ask for a more balanced committee with a broader diversity of views. A list of additions to the current provisional committee is below, submitted with details via “Feedback” on the IOM website. We feel that at least three candidates from this list should be named to the committee.

- Alan Greene, MD, FAAP, Stanford University School of Medicine, [agreene@DrGreene.com](mailto:agreene@DrGreene.com)
- Martha Herbert, MD, PhD, Harvard Medical School, [MHerbert1@PARTNERS.org](mailto:MHerbert1@PARTNERS.org)
- Irva Hertz-Picciotto, MA, PhD, MPH, University of California - Davis, [ihp@ucdavis.edu](mailto:ihp@ucdavis.edu)
- Mark D. Noble, PhD, University of Rochester Medical Center, [noble@urmc.rochester.edu](mailto:noble@urmc.rochester.edu)
- Issac N. Pessah, PhD, University of California - Davis, [inpessah@ucdavis.edu](mailto:inpessah@ucdavis.edu)
- Lawrence D. Rosen, MD, Hackensack University Medical Center, [ldrdoc@alum.mit.edu](mailto:ldrdoc@alum.mit.edu)
- Robert Sears, MD, FAAP, pediatrician, private practice, [Drbobsears@cox.net](mailto:Drbobsears@cox.net)
- Judy Van De Water, PhD, University of California - Davis, [javandewater@ucdavis.edu](mailto:javandewater@ucdavis.edu)

The committee should be free of conflicts of interest. One provisional committee member, Dr. Hugh Sampson, holds a patent for a vaccine against peanut allergy. Findings of adverse effects from vaccines might diminish the market potential for this vaccine and

would work against Dr. Sampson's financial interests. While we are not commenting on Dr. Sampson's impressive credentials or commitment, we respectfully request that he be removed from the panel.

5. Modify process for meetings and reports

We ask that public input be allowed on the selection of the presenters for the subsequent meetings, and that presenters represent a range of expertise, with an emphasis on basic science and not epidemiology. The epidemiological infrastructure available to the government for study, primarily VAERS and VSD, have weaknesses and are not open to independent scientists. Sufficient time should be scheduled for a wide variety of presentations and questions regarding exploration of gaps.

All meetings should be open to the public, not just the presentation meetings but the deliberation meetings as well. There is no overriding reason for closed deliberations and secrecy. Transcripts of all meetings should be made available in reasonable time to the public, including posting on the IOM website. FACA rules on committee communications should be followed even if not required by law.

"Community" reviewers should be included in the peer review process for final reports. The draft reports should be posted publicly for comment before finalization.

We are encouraged that HRSA has recognized the need to provide the Vaccine Court with more evidence on the adverse effects of vaccines in widespread use. Many of these vaccines have been licensed for years, in the case of Hepatitis B, almost two decades, and yet the nature and extent of the adverse effects of these products is still poorly understood. We hope the IOM will help to rectify this state of affairs by instituting an open, fair and rigorous review which will serve as a model for transparency, broad participation, balance, and independence.

Sincerely,



Sallie Bernard  
Executive Director

Cc Geoffrey S. Evans, Director, Division of Vaccine Injury Compensation, HRSA,  
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Judith A. Salerno, Executive Officer, IOM, [jsalerno@nas.edu](mailto:jsalerno@nas.edu)  
Kathleen Stratton, RSO, Adverse Effects of Vaccines Committee, IOM,  
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