# Memorandum

JAN 3 1992

Date

From Richard P. Kusserow
Inspector General For Bryan Mitchell

Subject Review of Alleged Conflict-of-Interest In Institute of Medicine Study of the Adverse Consequences of Pertussis and Rubella Vaccines (A-15-90-00054)

To James 0. Mason, M.D., Dr. P.H.
Assistant Secretary
for Health

The attached final audit report provides you with the opportunity to review and comment on our examination of internal control weaknesses involving a study mandated by the National Childhood Vaccine Injury Act (Public Law 99-660), enacted November 14, 1986, of the adverse consequences of the pertussis and rubella vaccines. In accordance with the Act, the Department of Health and Human Services' (HHS), National Institutes of Health (NIH), entered into an advisory and assistance service contract with the National Academy of Science (NAS). Under this contract, the Institute of Medicine (IOM) of the NAS was to perform this study.

Our review was requested by the Chairman of the Permanent Subcommittee on Investigations, Senate Committee on Governmental Affairs. The Subcommittee Chairman asked the Office of Inspector General (OIG) to examine a possible conflict-of-interest situation involving the IOM committee established to conduct the study of pertussis and rubella vaccines. The Subcommittee had received allegations regarding two committee members' conflicts-of-interest that could adversely affect the credibility of the study. One of these members resigned from the committee prior to our review.

We verified the existence of conflicts-of-interest situations for the two committee members. We also found that NIH did not follow Federal regulations to assure the impartiality and objectivity of work performed under an advisory and assistance contract.

In its reply to our draft report, the Public Health Service (PHS) concurred with our recommendations to evaluate possible conflicts-of-interest for all committee members and determine whether the work performed under this contract met Federal requirements to assure impartial and objective advice and assistance. The PHS also concurred with our recommendation to assure that all current and future advisory and assistance contracts with NAS or IOM require it to certify in writing that its organization has no conflicts-of-interest involving

PHS contracts and that the contracts should provide remedies for inadequate certification and the existence of a conflict-of-interest as determined by the contracting officer.

We would appreciate being advised within 60 days on the status of corrective actions taken or planned on each recommendation. If you wish to discuss the issues raised by our review, please contact me or your staff may contact Daniel W. Blades, Assistant Inspector General for Public Health Service Audits at (FTS)443-3583.

Department of Health and Human Services

# OFFICE OF INSPECTOR GENERAL

# REVIEW OF ALLEGED CONFLICT-OF-INTEREST IN INSTITUTE OF MEDICINE STUDY OF THE ADVERSE CONSEQUENCES OF PERTUSSIS AND RUBELLA VACCINES


Richard P. Kusserow
**INSPECTOR GENERAL,**

**A-15-90-00054**

# Memorandum

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Subject Review of Alleged Conflict-of-Interest In Institute of Medicine Study of the Adverse Consequences of Pertussis and Rubella Vaccines (A-15-90-00054)

To James 0. Mason, M.D., Dr. P.H.
Assistant Secretary
for Health

This final audit report addresses internal control weaknesses involving a study mandated by the National Childhood Vaccine Injury Act, (Public Law 99-660), enacted November 14, 1986, of the adverse consequences of the pertussis and rubella vaccines. In accordance with the Act, the Department of Health and Human Services' (HHS), National Institutes of Health (NIH), entered into an advisory and assistance service contract with the National Academy of Science (NAS). Under this contract, the Institute of Medicine (IOM)[1] is to perform a literature search and study to determine adverse side effects of the pertussis and rubella vaccines.

Our review was requested by the Chairman of the Permanent Subcommittee on Investigations, Senate Committee on Governmental Affairs. The Subcommittee Chairman asked the Office of Inspector General (OIG) to examine a possible conflict-of-interest situation involving the IOM committee established to conduct the study of pertussis and rubella vaccines. The Subcommittee had received allegations regarding two committee members' conflicts-of-interest that could adversely affect the credibility of the study.

We reviewed the documents IOM used to select members of the committee to study pertussis and rubella vaccines. We verified the existence of conflicts-of-interest situations for two of the committee members. One individual was employed by a nonprofit Fund that was fully supported by a pertussis manufacturer. Another resigned after IOM learned that the person had made public statements in a legal deposition on the effects of pertussis vaccines. The opinion expressed by this person prejudged the findings of this committee.

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'The IOM is one of three organizations under the jurisdiction of the NAS. A significant portion of NAS activities are performed under contract with the U.S. Government and are conducted by volunteer committees appointed for their special expertise in respective areas of study.

We found that NIH did not follow Federal regulations to assure the impartiality and objectivity of work performed under an advisory and assistance contract. Specifically, NIH did not obtain assurances from the contractor that conflicts-of-interest do not exist.

Although Federal regulations governing freedom from conflicts-of-interest were not included in the contract, IOM is responsible for completing an impartial and objective study. According to HHS' Office of General Counsel (OGC), this responsibility continues to be in effect because contractors must comply with all pertinent rules and regulations even if they are not specifically enumerated in the contract. In addition, the contract included a "Rights in Data" clause to allow NIH access to'documents needed to verify the objectivity of the study. However, despite NIH's attempts to obtain access to these documents, the IOM would not provide them under provisions of this clause.

In a previous OIG report, "Departmental Controls Over Obligations For Advisory and Assistance Services Need to Be Strengthened," issued on February 25, 1991, we reported internal control weaknesses in HHS controls to avoid potential conflicts-of-interest. We recommended that the Department institute a system to inform contractors and, perhaps, potential contractors, of possible conflict-of-interest matters. In accordance with regulatory requirements to heighten accountability among contractors, we recommended that contractors certify that they have been apprised of and comply with guidelines. The HHS generally concurred with our recommendations and agreed to implement Federal Acquisition Regulations requiring certification for advisory and assistance contracts.

On May 10, 1991, we briefed NIH officials about our findings. They agreed with our finding regarding the appearance of conflicts-of-interest for the two committee members. They also agreed that NIH failed to follow Federal regulations to assure the impartiality and objectivity of services provided through advisory and assistance contracts. In Public Health Service's (PHS) October 30, 1991 response to our draft report, it fully agreed with our recommendations and stated that corrective actions have been taken or are planned for implementation.

## BACKGROUND

Our review was performed in response to a congressional request indicating specific concerns about the appearance of conflicts-of-interest in a study funded by NIH. Public correspondence received by the subcommittee indicated that conflicts-of-interest existed for two committee members.

However, one of these members resigned from the committee prior to our review.

The National Institute of Allergy and Infectious Diseases (NIAID), 1 of 12 institutes within NIH, is responsible for carrying out the requirements of the "National Childhood Vaccine Injury Act." This Act provides compensation to the public for adverse reactions occurring from mandatory vaccine immunizations given to children. Section 312 of the Act, mandated a study to determine if adverse reactions occur after the pertussis and rubella vaccines are administered and to evaluate if these vaccines should be refined or eliminated.

The Act directed NIH to study the pertussis and rubella vaccines through an advisory and assistance contract with IOM. The contract, 1 of 10 advisory and assistance contracts currently being performed for the Public Health Service, was signed on September 27, 1989. The contract with the NAS calls for IOM to perform a a-year, $580,000 literature search of all data compiled about pertussis and rubella use, for the purpose of determining if significant adverse side effects result from administration of the vaccines. As of May 2, 1991, IOM had received approximately $475,800 in payment for work performed.

There are numerous conflict-of-interest prohibitions that apply to organizations or individuals performing advisory and assistance contract services.

The OMB Circular A-120, regulating advisory and assistance service contracts, states that appropriate disclosure be required of, and warning provisions issued to, consultants and experts to avoid conflict-of-interest. This Circular further requires agencies, such as NIH, to properly administer and monitor these contracts to ensure that performance is satisfactory.

The Office of Federal Procurement Policy in its Policy Letter 89-l defines conflict-of-interest as "that condition or circumstance wherein a person is unable or is potentially unable to render impartial assistance or advice to the government because of other activities or relationships with other persons, or wherein a person has an unfair competitive advantage." According to the Policy Letter, a conflict-of-interest would occur if the person evaluating a contractor's, or potential contractor's, products or services, is or was substantially involved in the development or marketing of those products or services. In addition, the Policy Letter further indicates that responsibility for identifying and preventing potential conflicts-of-interest in government contracts, rests with, among others, the government contracting officer.

Federal Acquisition Regulations (FAR) require contracting officers to identify and evaluate potential organizational conflicts-of-interest as early in the acquisition process as possible: and avoid, neutralize or mitigate significant potential conflicts before contract award. FAR (48 C.F.R.) Section 9.504. These regulations further direct that, if a potential conflict exists, contracting officers include an approved solicitation provision and contract clause in the contract. FAR (48 C.F.R.) Section 9.508.

In an effort to detect possible conflicts, the IOM requires potential committee members to submit both a Curriculum Vitae (CV), and a "Potential Sources of Bias and Conflict of Interest" statement. These documents provide the IOM with the applicant's employment history, as well as their outside arrangements, agreements, and investments. Moreover, these records identify the applicant's qualifications and outside interests that could conflict or potentially conflict with work performed for the committee.

## OBJECTIVES, SCOPE, AND METHODOLOGY

The objectives of this review were to: (1) determine if conflicts-of-interest existed for the two IOM committee members that were the focus of allegations received by the Subcommittee; and (2) evaluate whether NIH met Federal requirements to assure the receipt of an impartial and objective product.

To identify the possible existence of conflicts-of-interest, we examined information included in documents committee members were required to submit to IOM during the application process and annually thereafter. We also evaluated NIH contracting procedures by reviewing applicable Federal regulations, as well as the contract awarded to IOM. In addition, we interviewed personnel from NIH and the IOM to gain a perspective on policies and procedures in place to ensure receipt of an impartial product. We obtained comments from OGC regarding our review of the conflicts-of-interest for the two committee members that were the focus of allegations received by the Subcommittee. We performed a limited review of IOM procedures for selecting the study committee members. The study was not completed during our review. Therefore, we could not examine the study results.

Our review was conducted between August 1990, and February 1991, at the NIH campus in Bethesda, Maryland and the IOM in Washington, D.C., in accordance with generally accepted Government auditing standards.

TWO IOM COMMITTEE MEMBERS HAD CONFLICTS-OF-INTEREST

We determined that there were two conflict-of-interest situations that could adversely affect the pertussis study findings. One conflict resulted from a committee member's receipt of a 5-year stipend totalling $300,000 from a nonprofit medical research Fund wholly supported by a major pertussis manufacturer. The committee member disclosed the stipend on the bias statement submitted to IOM and, after reviewing this documentation, IOM concluded that there was no conflict-of-interest. According to IOM, no conflict-of-interest existed because the stipend from the nonprofit Fund "did not connect" the individual with the pertussis manufacturer. However, we determined that this Fund, wholly supported by the pertussis manufacturer, is composed of senior-level managers employed by the pertussis manufacturer. We also found that the Fund is directly involved in selecting the recipient, and funding that individual's research. The fact that the study conclusions could have a direct financial effect on this pertussis manufacturer raises questions about the committee member's ability to be an impartial and objective participant. Moreover, even in the absence of any direct financial link to the outcome of the research, the committee member's objectivity could be compromised by a sense of loyalty to the pertussis manufacturer.

The second conflict-of-interest was identified by outside sources prior to our review. At IOM's request this committee member resigned after IOM learned that the person had made public statements in a legal deposition on the effects of pertussis vaccines. In addition, this committee member had not disclosed these remarks on the required documentation submitted for IOM's review.

NIH DID NOT ENFORCE FEDERAL CONTRACT REGULATIONS

The NIH did not meet Federal requirements for assuring the objectivity and impartiality of services provided through advisory and assistance contracts. Numerous conflict-of-interest prohibitions apply to organizations or individuals performing advisory and assistance contracts. For example, OMB Circular A-120 requires appropriate disclosure and the issuance of warning provisions to contractors to avoid conflicts-of-interest. The Federal Acquisition Circular requires that contractors certify in writing that officers or employees have no information concerning a violation or possible violation of Federal conflict-of-interest requirements. However, NIH did not include these requirements in the contract with IOM. Further, a "Rights in Data" clause providing access to the contractor's documents, was included in the NIH contract. Despite NIH's attempts to use this

clause to obtain access to documents, IOM would not provide these documents.

FEDERAL CONFLICT-OF-INTEREST REGULATIONS IN EFFECT EVEN THOUGH NOT INCLUDED IN THE CONTRACT

Omission of Federal regulatory requirements in its contract governing freedom from conflicts-of-interest does not diminish IOM's responsibility for completing a study that results in impartial and objective study findings. This responsibility continues to be in effect, because contractors must comply with all pertinent rules and regulations regardless of whether they are specifically enumerated in contract documents.

CONCLUSIONS AND RECOMMENDATIONS

Public concerns about the existence of conflicts-of-interest for two committee members appear to be justified. In fact, the selection of two committee members who were not impartial reflects a weakness in NIH policies and procedures designed to identify and exclude applicants who had conflicts-of-interest.

The NIH did not include Federal regulatory requirements governing assurances of the impartiality and objectivity of work performed in its contract with IOM. In addition, NIH included a contract clause providing access to documents submitted to IOM, but was not able to obtain these documents. Although Federal regulations governing freedom from conflicts-of-interest were not included in the contract, IOM is responsible for completing an impartial and objective study.

Based on our finding that a conflict-of-interest appears to exist, NIH needs to determine if an impartial, objective product is being provided in accordance with Federal regulations. If NIH determines that the committee's work did not result in impartial study conclusions, NIH should take appropriate actions. These actions may include removal of committee members shown to have conflicts-of-interest, recovery of Federal funds, and any other actions deemed necessary.

We therefore recommend that you direct NIH to:

1. Evaluate possible conflicts-of-interest.,for all IOM committee members and take corrective action including removal if necessary.

2. Determine whether the work performed under this contract meets Federal requirements to assure impartial and objective advice and assistance. If not, NIH should take appropriate corrective action.

3. Assure that all current and future advisory and assistance contracts with NAS or IOM requires it to certify in writing that its organization has no conflicts-of-interest involving Public Health Service contracts. The contract should also provide remedies for inadequate certification and the existence of a conflict-of-interest as determined by the contracting officer.

AGENCY COMMENTS AND OIG RESPONSE

The PHS, in its October 30, 1991, comments on our draft report, generally concurred with our recommendations. Its complete response is included in its entirety as Appendix A to this report and certain responses are paraphrased in this section.

The PHS concurred with our recommendations to evaluate possible conflicts-of-interest for all committee members and determine whether the work performed under this contract met Federal requirements to assure impartial and objective advice and assistance. Following OIG's review and briefing of NIH officials, NIH conducted a preliminary review and concluded that although no actual conflict-of-interest existed, the appearance of a conflict-of-interest did exist for both committee members identified by the OIG. The NIH took additional actions to ensure impartiality and objectivity of the IOM committee process and report by having an outside expert evaluate whether there were conflicts-of-interest and biases that affected the validity of the study. The expert found no evidence of any conflict-of-interest, either in the report or the processes of the IOM committee. However, PHS comments did not indicate if they evaluated conflicts-of-interest for all IOM committee members as recommended.

The PHS concurred with our recommendation to assure that all current and future advisory and assistance contracts with NAS or IOM requires it to certify in writing that its organization has no conflicts-of-interest involving PHS contracts and that the contracting officer should provide remedies for inadequate certification and the existence of a conflict-of-interest as determined by the contracting officer. The NIH modified the IOM contract in May 1991 to include a special conflict-of-interest clause applicable to NAS and IOM. In addition, steps have been taken to ensure that all future advisory and assistance contracts follow the Federal regulations implemented on October 22, 1990 and result in the provision of impartial and objective advice and assistance. Specific guidance is also being issued by NIH to address the contracting officer's responsibility in verification of conflicts-of-interest in advisory and assistance and other contracts.

We would appreciate being advised within 60 days on the status of corrective'actions taken or planned on each recommendation. If you wish to discuss these issues further, please contact me or your staff may contact Daniel W. Blades, Assistant Inspector General for Public Health Service Audits at (FTS)443-3583.

Appendix A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

# Memorandum

Date · OCT 30 1991

From Assistant Secretary for Health

Subject Office of Inspector General (OIG) Draft Report "Review of Alleged Conflict-of-Interest in Institute of Medicine Study of the Adverse Consequences of Pertussis and Rubella Vaccines"

To Inspector General, OS

Attached are the Public Health Service comments on the subject OIG draft report. We concur with each of the report's recommendations and our comments delineate the actions we have taken or plan to take to implement them.

James O. Mason

James O. Mason, M.D., Dr.P.H.

Attachment

| | |
|---|---|
| IG | ✓ |
| PDIG | ✓ |
| DIG-AS | ✓ |
| DIG-EI | |
| DIG-OI | ✓ |
| AIG-MP | ✓ |
| OGC/IG | ✓ |
| EXSEC | |
| DATE SENT | 11/1 |

# PUBLIC HEALTH SERVICE (PHS) COMMENTS ON THE OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT "REVIEW OF ALLEGED CONFLICT-OF-INTEREST IN INSTITUTE OF MEDICINE STUDY OF ADVERSE CONSEQUENCES OF PERTUSSIS AND RUBELLA VACCINES," A-15-90-00054

## General Comments

This report summarizes the OIG's review of alleged conflict-of-interest in an advisory and assistance contract with the Institute of Medicine (IOM). The National Institute of Allergy and Infectious Diseases of the National Institutes of Health (NIH) entered into this contract on behalf of the Department to fulfill the requirements of Section 312 of Public Law 99-660. The contract provided support for IOM to establish and provide staff support for a committee of experts to study available evidence gleaned from scientific literature and expert opinion about the adverse consequences of pertussis and rubella vaccines.

The report identifies two issues: (1) conflict-of-interest for two members of the IOM committee, and (2) failure of NIH to follow Federal regulations to ensure impartiality and objectivity of work performed under an advisory and assistance contract.

## OIG Recommendation

We recommend that the Assistant Secretary for Health direct NIH to:

1. Evaluate possible conflicts-of-interest for all IOM committee members and take corrective action including removal if necessary+

## PHS Comment

We agree that even the appearance of conflict-of-interest must be avoided for studies with such important impact on the public health of this country. NIH has concluded that an appearance of conflict-of-interest existed in both cases identified by OIG, with the first case being clearly more significant'than the second. In the first case, a committee member failed to report testimony given in a deposition that clearly stated his views about the possibility of adverse reactions associated with the *use* of the pertussis vaccine. The situation presented a clear bias on the part of that individual. This fact was exposed by interested parties outside of the IOM process at the first public meeting of the committee in January 1990.

The process established by IOM to safeguard against conflict-of-interest failed to detect the potential problem. However, IOM verified the charge promptly, and the expert resigned from the committee immediately. Since the committee process had just begun, NIH concluded that the expert's limited participation did not bias the work of the committee. The quick action of IOM and

the prompt resignation of the member precluded any real or perceived bias in the preparation of the report.

In the second case, IOM ruled that the source of a stipend for a committee members' post-doctoral fellowship, which was reported to IOM in advance of her appointment to the committee, did not give an appearance of conflict-of-interest, NIH was not informed of this information at that time. The expert continued to serve on the committee, which had almost completed its work by the time OIG staff briefed NIH officials on this draft report.

When information about the potential conflict-of-interest surfaced, another IOM review concluded that no appearance or actual conflict-of-interest existed. Following OIG's investigation and briefing of NIH officials, NIH conducted a prelimihary review, NIH concluded that no actual conflict-of-interest existed, although the appearance of a conflict did exist.

The basis for the charge in the second case rests on the relationship between the expert and the source of her fellowship stipend. The expert was awarded a post-doctoral fellowship in pharmacoepidemiology following a fair and open competition. She was selected by an independent panel. of experts organized by a professional society with no ties to the vaccine industry. The fellowship is funded by a non-profit trust in the United States (U.S.) that is fully supported by a U.S. pharmaceutical firm with no commercial interest in vaccines.

Although the U.S. firm that funds the foundation is a subsidiary of a firm in the United Kingdom (U.K.) that formerly manufactured pertussis vaccine, and most of the board members of the foundation are senior scientists and executives of the U.K. firm, their pertussis vaccine was never licensed or marketed in the U.S. The linkage between the expert and commercial interest in pertussis vaccine is sufficiently indirect to preclude *any* actual conflict-of-interest.

NIH found no plausible direct link between the expert and commercial interests in pertussis-vaccine. The actions of the expert in the IOM process would not affect her *interests or* those of a company which could not exert control over her by reason of employment or consulting relationship, However, NIH agrees that there was an appearance of conflict that required an in-depth investigation to fully comprehend.

NIH took additional actions to ensure the impartiality and objectivity of the IOM committee process and report. It is important to remember that the IOM committee released its report one month before the Inspector General issued his report. Therefore, NIH thought it appropriate to have an outside expert

review the IOM report and committee process to evaluate whether there were conflicts-of-interest and biases that affected the validity of the study. These actions are described in detail in the PHS comments section following recommendation number 2 below.

OIG Recommendation

2. Determine whether the work performed under this contract meets Federal requirements to assure impartial and objective advice and assistance.

**Office of Audit Services note -- comments have been deleted at this point because they pertain to material not included in this report.**

**PHS Comment**

We concur. NIH obtained the services of a prominent expert to examine closely both the IOM process and the committee's report for evidence of any manifestation of bias. Dr. Martha Yow, a former editor of The Journal of Infectious Diseases, was asked to review the IOM pre-publication draft of the report and the processes IOM used to manage the work of the committee. Dr. Yow was chosen because she is, a respected infectious disease physician with no direct ties to IOM, In addition, as an editor of a prominent medical journal, she is familiar with potential conflicts-of-interest that emerge in peer reviewing and publishing results of medical research articles that may have a significant impact on pharmaceutical firms. Her background in the field of infectious diseases and her practical experience with the ethical issues raised in this report provide a valuable, objective opinion about the degree to which the final IOM report may be biased by any appearance of conflict-of-interest.

Dr. Yow completed her work in August 1991 and found no evidence of any conflict-of-interest, either in the report or the processes of the IOM committee.

OIG Recommendation

3. Assure that all current and future advisory and assistance contracts with NAS or IOM requires it to certify in writing that its organization has no conflicts-of-interest involving PHS contracts. The contract should also provide remedies for inadequate certification and the existence of a conflict-of-interest as determined by the contracting officer.

PHS Comment

We acknowledge that NIH did riot include the specific Federal regulations tc ensure impartiality and objectivity in its contract with IOM. However, at the time the IOM contract was awarded {October 25, 1989) the Federal Acquisition Regulation Section 9.5, Organizational and Consultant Conflicts of Interest, did not require consultant certification under advisory and assistance service contracts. *The* regulations requiring these certifications were implemented on October 22 1990. Only solicitations issued after the effective date'of the regulations were affected by the certification requirements. Notwithstanding this, NIH modified the IOM contract on May 24, 1991, *to* include a special conflict-of-interest clause applicable to NAS and IOM.

In addition, steps have been taken to ensure that all future advisory and assistance contracts follow the Federal regulations implemented on October 22, 1990, and result in the provision of impartial and objective advice and assistance. NIH is issuing NIH-specific guidance to address the contracting officer's responsibility in verification of conflicts-of-interest in advisory and assistance or other contracts. This action has been coordinated with the HHS Office of Acquisitions and Grants Management.