DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control and Prevention

February 13, 2004

Leigh Pruneau, Ph.D., R.N.
IRB Administrator
Northern California Kaiser Permanente
1800 Harrison Street
16th Floor
Oakland, California 94162

RE: Protocol # CN-03MGeie-01-H

Dear Dr. Pruneau:

My office in the National Immunization Program has oversight responsibility for IRB issues related to research sponsored by the National Immunization Program. This letter is to inform you that my office has received reports from the technical monitors that accompanied Dr. Mark Geier and Mr. David Geier on their October 2003 and January 2004 visits to the Centers for Disease Control and Prevention's (CDC) Research Data Center (RDC) in Hyattsville, Maryland. These investigators were approved by your Institutional Review Board to conduct analyses in our RDC. These reports describe potential breaches in confidentiality and execution of analyses that were not approved in advance. Below is a synopsis of the key issues on these two topics.

From the October 9-10, 2003 Visit to the RDC

Protocol Issues

The approved analysis was to answer the following questions:

1. Does acellular DTaP increase the risk for acute adverse event (list of 15) within 30 days following vaccination?
2. Does acellular DTaP increase the risk of chronic adverse event (same list of 15) within 1 year following vaccination?

Instead, the Geiers compared autism rates in those receiving 100 mg of thimerosal from DTaP to those receiving zero mg from DTaP.

From the January 29-30, 2004 Visit to the RDC

Protocol Issues

The researchers asked how to merge datasets across studies to create a composite data file. They were told the files were not set up for such a merger and that such a merger was not part of the

approved analysis. Nevertheless, the researchers ran a program which attempted to merge datasets, and the visit ended with a cancellation of a SAS program that had been running for more than 45 minutes and was intended to have more than 8 million records in it (according to the programmer).

Confidentiality Concerns

By attempting to merge data files, the researchers would have created more complete medical records on subjects, and if so, could have increased the risk of a breach of confidentiality.

External researchers are provided with a copy of their SAS programs at the conclusion of their visit to the RDC. On this occasion, the external researchers attempted renaming data files with the ".sas" extension reserved for program files. This would have allowed the external researchers to remove data files from the RDC, contrary to the rules of the RDC. The violation was detected and only the correct files were ultimately released. The programmer stated that the files were created by mistake.

In summary, during the first visit the researchers conducted unapproved analyses on their datasets and on the second visit attempted to carry out unapproved analyses but did not complete this attempt. This analysis, had it been completed, could have increased the risk of a confidentiality breach. Before leaving, the researchers renamed files for removal which were not allowed to be removed. Had it gone undetected, this would have constituted a breach of the rules about confidentiality.

Please note, I have sent copies of this letter to Dr. Jared Rowe, IRB Administrator at Kaiser Permanente Colorado and Dr. Eric France, Principal Investigator for CDC's Vaccine Safety Datalink Project at Kaiser Permanente Colorado as well as Dr. Steve Black and Dr. Henry Shinefield, Co-Principal Investigators for CDC's Vaccine Safety Datalink Project at Northern California Kaiser Permanente. I have also sent copies of this letter to Kristina Borror, Director of Compliance at the Office of Human Research Protections. I was not able to send a copy to the sponsor of this research as we could not identify the sponsor.

Please inform us of actions, if any, you take in regard to these matters.

Sincerely,

Jeanne M. Santoli

Jeanne Santoli, M.D.
Acting Associate Director For Science
National Immunization Program
Centers for Disease Control and Prevention

cc:
Jared Rowe, Pharm.D
Eric France, M.D., M.S.P.H.
Steve Black, M.D.
Henry Shinefield, M.D.
Kristina Borror
Dixie Snider, M.D., M.P.H.
Ann Dellinger, Ph.D., M.P.H.

K · F · R · I
KAISER FOUNDATION
RESEARCH INSTITUTE

February 25, 2004

Mark Geier, MD
Principal Investigator
The Genetic Centers of America
14 Redgate Court
Silver Springs, Maryland 20905

Re: A Series of Studies to Analyze the Vaccine Safety Database (VSD)

Dear Dr. Geier:

On February 19, 2004, the Kaiser Permanente Northern California (KPNC) Institutional Review Board (IRB) **suspended your research project pending the following:**

- Submission of a response from you to the attached letter, which the Centers for Disease Control and Prevention (CDC) recently sent to the IRB notifying it of reports received from the technical monitors who accompanied you on visits to the CDC Research Data Center (RDC).

Please note: the IRB views with great concern the reported attempt to breach confidentiality and your attempts to merge data and conduct analyses which were not in accord with CDC procedures.

Also note: as a result of this suspension, you and your co-investigator are prohibited, until notified otherwise, from accessing VSD data derived from Colorado Kaiser Permanente and Northern California Kaiser Permanente.

Federal regulations and KPNC IRB policy prohibit the conduct of research that has been suspended by the IRB. The IRB is required to report, and will proceed to report, the suspension of this study to the CDC and Kaiser Permanente institutional officials.

The following actions are required:

- You must immediately cease all activities which involve Kaiser Permanente data, as is required by federal regulations and KPNC IRB policy.
- You must inform the IRB of any research-related activity continued beyond this notification of study suspension, providing the reason(s) for continuation.
- You must provide written notification of study suspension and the required cessation of all research activities to the co- and sub- investigators, if any, participating in this research within five business days of receiving this notification.

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The IRB requires that you provide your response to the CDC's letter to KFRI via e-mail to KPNC IRB on Lotus Notes, or KPNC.IRB@kp.org, or by U.S. mail by noon on March 8, 2004, for review at the March 18, 2004 IRB meeting.

Sincerely,

Leigh Pruneau, PhD, RN
KPNC IRB Administrator

cc: Armida Ayala, PhD
IRB Administrator
Kaiser Permanente Southern California
Steve Black, MD
Co-Principal Investigator
CDC Vaccine Safety Datalink Project
Kaiser Permanente Northern California
Kristina Borror
Director of Compliance
Office of Human Research Protections
Eric France, MD
Principal Investigator
CDC Vaccine Safety Datalink Project
Kaiser Permanente Colorado
David Geier
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David Holt, JD
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Jared Rowe, PharmD
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Nancy King, MPH, MEd
Vice President - Kaiser Permanente
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Jeanne Santoli, MD,
Acting Associate Director for Science
National Immunization Program
Centers for Disease Control and Prevention
Henry Shinefield, MD
Co-Principal Investigator
CDC Vaccine Safety Datalink Project
Kaiser Permanente Northern California

March 1, 2004

Leigh Pruneau, Ph.D., R.N.
IRB Administrator
Northern California Kaiser Permanente
1800 Harison Street
16th Floor
Oakland, CA 94162

Re: A Series of Studies to Analyze the Vaccine Safety Datalink Database (VSD)

Dear Dr. Pruneau,

We are in receipt of your letter of February 25, 2004 informing us that access to the Vaccine Safety Datalink Data ("VSD") derived from Colorado Kaiser Permanente and Northern California Kaiser Permanente ("CKP") and ("NCKP") has been suspended based upon a report from the Centers for Disease Control ("CDC") alleging that we have: 1) executed analyses outside of the IRB approved protocol; and 2) purposefully acted to breach patient confidentiality by "merging datasets across studies to create a composite data file). See, February 13, 2004 letter from Jeanne Santoli, M.D, Acting Associate Director For Science, National Immunization Program, CDC. We categorically deny these baseless allegations made by Dr. Santoli for the reasons set forth below:

I. Analyses Were Not Conducted Outside of the IRB Approved Protocol

The IRB approved protocol contained two hypotheses. The first hypothesis focused on whether or not there was an increased risk for an acute adverse event (list of 15) within thirty (30) days after vaccination with acellular DtaP. The second hypothesis focused on whether or not there was an increased risk for a chronic adverse event (same list of 15) within one year after vaccination with acellular DtaP.

As way of background, the datasets assembled by CDC contain no names, addresses, zip code, state of residence, phone number, HMO membership information or center of examination for each patient. In addition, ***patients are identified by an encrypted randomly assigned patient number that is different for each dataset. No dataset contains more than one vaccine administered and one patient could have numerous randomly assigned patient identification numbers.***

In the brief time we were able to access the VSD data on October 9-10, 2003 CDC allowed us to access datasets with the following information per patient identifier number: specific vaccine and brand name, ICD-9 code and date of diagnosis assigned, maternal age, APGAR score at birth, birthweight, gestation and race. The ICD-9 codes were limited to 15 set forth in the approved IRB protocol. We are currently in the process of analyzing the temporal relationship between the administration of the vaccine and these 15 ICD-9 codes. Therefore, for CDC to allege that we have violated the protocol is disingenuous since we have not even been allowed to finish our analysis.

Further, since different brand name vaccines are used, it is not violative of the protocol to examine whether or not an acute or chronic condition is associated with a specific vaccine and not accellular DtaP vaccines in general. If a statistically significant relationship is found based upon the brand of vaccine administered this information should be vitally important to you as well as the CDC.

II. Merging Datasets is an Impossibility

The VSD dataset prepared for us reside at the CDC's Research Data Center (RDC) in Hyattsville, Maryland. The RDC has armed guards at the front door. No one is allowed to enter the building except by pre-arranged identification of persons to the RDC staff and subsequent escort by RDC staff to specific specially designed research rooms. There are defined researcher hours to access the RDC.

There are only three people that have been granted access to our CDC prepared VSD dataset including: Dr. Mark R. Geier (Principal Investigator), David A. Geier (Co-Investigator), and Vale Krenick (Computer Programmer).

The research rooms have keypad locked entry, and have no communicative equipment to allow researchers to be able to contact anyone outside the RDC. No researcher may bring in cell phones, pagers, or other recording equipment while inside the research room.

In the actual research room RDC monitors stand fulltime guard (we have had three different monitors while accessing the VSD database, most recently we had two monitors watch us in a single session). There is a single computer in the research room with our CDC prepared VSD dataset pre-loaded onto the hard-drive. The computer's disk drive is disabled during the time we are permitted to analyze the VSD dataset.

In printing-out information from the VSD database, our printouts are produced on a printer in a separate locked room, and a completely independent staff member of the RDC is the only one who has access to our printed materials. The protocol for looking at print-outs requires that the independent staff member with access to the print room be retrieved, so that this individual may then pass the printouts onto the monitors in the research room. The monitors in the research room prevent any information that may endanger patient confidentiality from leaving the research room by obliterating the material on the printouts. They then take the print-outs and photocopy them, so as to ensure that any process that may be undertaken by the researchers to attempt to unobliterate the printouts is impossible.

The monitors ensure at the end of each session that no actual VSD raw data is exported from the VSD in digital, printed, or written form.

It is impossible for the datasets given to us by CDC to be merged. As stated previously each dataset contains encrypted randomly assigned patient identifiers. It is impossible therefore to construct a dataset that contains any information on one patient that links the vaccines administered to the ICD-9 diagnosis. It should be pointed out that CDC and its

approved external researchers have full access to this type of information, not us. In fact, there is a "two-tiered" research approach at CDC. If a researcher is part of the VSD "team" they can access all data freely (including downloading data and removing it from the RDC with minimum patient confidentiality protection). Further, it is our understanding that VSD "team" researchers do not have to obtain IRB approval for studies.

Dr. Santoli's letter alleges during a visit to the data center on January 29-30, 2004 we "ran a program which attempted to merge datasets and the visit ended with cancellation of a SAS program that had been running for more than 45 minutes and was intended to have more than 8 million records in it." This is simply not true. What we were attempting to accomplish was to merge the datasets given to us by CDC to build a record containing the following information on a patient: race, sex, date of vaccination, name brand of vaccine used, date of ICD-9 code assignment if given, birthweight, APGAR, maternal age and gestation. The computer available for us at the research data center is obsolete and is completely inadequate to even analyze the information contained in a single vaccine dataset thus the reason for the 45 minute delay.

In addition, Dr. Santoli's letter further alleges that "the external researchers attempted renaming the data files with the ".sas" extension reserved for program files…The violation was detected and only the correct files were ultimately released". We acknowledge that this file was made in error and in fact, it was our computer programmer who ***pointed out this error to the CDC***.

We hold patient confidentiality with the utmost regard, and have done everything within our power to ensure patient confidentiality within our prepared VSD dataset. The CDC letter presents no information showing that we have attempted in any way to violate the confidentiality of patients from NCKP. The RDC of the CDC has a highly developed protocol to ensure that it is virtually impossible to breach patient confidentiality. Additionally, the VSD dataset prepared for us by the CDC contains no names, addresses, zip codes, states of residence, phone numbers, HMO membership information, or centers for examination at each HMO for each patient making breaches in patient confidentiality virtually impossible.

One final note, we were asked by members of Congress to investigate the VSD, especially with regards to the thimerosal and neurodevelopmental disorder issue. Therefore, we were only doing the study which the Congress asked us to do, and which the CDC agreed to cooperate to allow us to do. We resent the implication that we would try, even if we could, which we could not, to breach patient confidentiality. We have always and will continue to guard patient confidentiality with the greatest care. We would appreciate a timely restoration of our access to the VSD in order to continue our scientific work.

Sincerely

Dr. Mark R. Geier

David A. Geier