ORIGINAL

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

OFFICE OF SPECIAL MASTERS

IN RE: CLAIMS FOR VACCINE INJURIES RESULTING IN AUTISM SPECTRUM DISORDER, OR A SIMILAR NEURODEVELOPMENTAL DISORDER,

Various Petitioners,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

PSC SECOND MOTION TO COMPEL VSD ACCESS

AUTISM MASTER FILE

Special Master George Hastings

PETITIONERS' MOTION TO COMPEL AND FOR ISSUING THIRD-PARTY SUBPOENAS

Pursuant to Vaccine Rule 7 (b) and (c), RUSCC 34, and RUSCC 45, petitioners move the Special Master to:

1) Issue an Order compelling the respondent to give petitioners and petitioners' experts access to the Vaccine Safety Datalink (VSD) for purposes of an investigation into potential associations between thimerosal and MMR exposure and adverse neurological or developmental outcomes in children; and

2) Issue subpoenas to all participants in the VSD program, including any Managed Care Organizations (MCOs) and contractors with custody of the data in issue, requiring those third parties to give petitioners and petitioners' experts access to the VSD for purposes of an investigation into potential associations between thimerosal and MMR exposure and adverse neurological or developmental outcomes in children, pursuant to RUSCC 45.

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MEMORANDUM IN SUPPORT OF PSC MOTION TO COMPEL

A. Introduction

The Vaccine Safety Datalink (VSD) is a significant source of data that can help shed light on the issues faced by the Special Master in this Omnibus Autism proceeding: whether there is epidemiological evidence of a causal association between doses of thimerosal in infant vaccines, or doses of the MMR vaccine, and neurological disorders on the autism spectrum.

Access to the Vaccine Safety Datalink has been an ongoing subject of the PSC's discovery requests. The PSC first requested relevant VSD data in Requests for Production served in August 2002. Respondent objected, and petitioners in March 2004 filed a Motion to Compel seeking an Order directing the CDC to allow petitioners and their experts access to the VSD in order to conduct research into thimerosal and MMR exposure and adverse health outcomes. In its filings with the Special Master and in testimony at hearings on the earlier Motion, respondent indicated that its client agencies were no longer in "possession or control" of the VSD,[1] arguing that the agencies therefore could not comply either with a request for the production of the VSD, or with an order compelling the agencies to provide access to the VSD. In the course of briefing and arguing the Motion to Compel, the PSC learned that the CDC had contracted with a third-party vendor (America's Health Insurance Plans, or AHIP) to manage and administer the VSD, creating the impression that the CDC no longer had "possession or control" of the VSD. Believing that the evidence in late 2004 indicated that the CDC no longer had "possession or control" of the VSD, petitioners filed an Amended Motion to Compel (April 8, 2005), withdrawing the request for VSD access but explicitly reserving the right to reassert the request at a later time.

As will be detailed in this Memorandum, the ability of external researchers (that is, researchers not employed by the CDC or the MCOs) to conduct studies involving the VSD is

[1] *See,* "Respondent's Response to Petitioners' Motion to Compel," May 14, 2004, p. 19, fn 16 and p. 23, fn. 19; also, "Respondent's Supplemental Response to Petitioners' Motion to Compel," June 15, 2004, p. 37.

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governed in large part by the CDC and its related entities, including the Research Data Center of the National Center for Health Statistics, and is conducted pursuant to procedures established and administered by the CDC.[2]

The CDC's very active role in regulating any and all access to the VSD, in short, clearly demonstrates that while the agency may no longer have "possession" of the VSD itself, the agency continues to assert meaningful "control" over the database in a manner that makes the CDC appropriately subject to an Order of the Special Master compelling the agency to make the VSD available to the petitioners' experts. It is for this reason that the PSC renews and narrowly focuses its earlier Motion to Compel. The PSC proposes a very specific investigation to be conducted upon the CDC's provision of access to the VSD. That proposal is attached as Exhibit 86 to this Motion and Memorandum. The same research proposal would govern the PSC's access to the VSD when provided by the participating MCOs pursuant to the subpoenas requested by petitioners in this Motion.

The PSC is aware of the absence of precedent in the Vaccine Program for such an Order and subpoenas. However, the PSC notes that the Vaccine Program's congressional mandate is "to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines." 42 U.S.C. 300aa-1. In other words, Congress intended to encourage the development of safe vaccines by 1) limiting civil lawsuits against vaccine manufacturers and 2) fairly compensating persons likely injured by vaccines. By granting this motion, the PSC submits, the Special Master will promote both goals of Congress. Simply put, granting access to this crucial data will provide nearly 5,000 neurologically and neurodevelopmentally injured children with their best chance of success in

[2] Between April 2005 and August 2006, petitioners sought access to the VSD by working directly with researchers who had already initiated a series of vaccine safety studies pursuant to approval by the Institutional Review Boards (IRBs) of some of the managed care organizations (MCOs) participating in the VSD. Those studies, however, were not explicitly designed to investigate an association between thimerosal exposure and pediatric neurological or developmental injuries, as is the case with the proposed study in this Motion. The CDC and the MCOs refused to allow the researchers involved in those ongoing studies to combine datasets for multiple vaccines, and in August 2006 the CDC terminated the ongoing research by those investigators, seized work product already generated, and barred ongoing access to the VSD by the researchers.

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the Program and obviate the need for civil lawsuits to secure access to the data. Denial of the PSC's motion, on the other hand, not only will deny these autistic children the "fundamental fairness" required by Vaccine Rule 8 (c), but also may provide the basis for a motion for review under 300aa-12 (e) (2)(B).

Finally, results of the proposed study are "reasonably necessary" to the Special Master's general causation inquiry, as described in petitioners' earlier Motion, and as will be detailed below.

B. The Special Master is Authorized to Conduct the Discovery Requested by Petitioners

1. The Special Master has Explicit Authority to Conduct Discovery Involving Parties to a Compensation Proceeding.

Both the Vaccine Act and the Vaccine Court Rules explicitly authorize the Special Masters to conduct discovery in a proceeding on a petition for compensation. 42 U.S.C. §300aa-12(d)(3)(B); Vaccine Rule 7(b) (authorizing the use of the "discovery procedures provided by RCFC 26 – 37" in Vaccine Court proceedings). The Special Master is granted considerable flexibility and discretion to investigate the facts of any claim in the program, including the ability to order discovery. It therefore matters little that discovery is not available "as a matter of right," so long as petitioners can convince the Special Master that the requested discovery—including the production of any documents such as data files or data sets—is "reasonable and necessary" to resolving a material issue in a compensation claim. 42 U.S.C. §300aa-12(d)(3)(B).

2. The Special Master is Authorized to Conduct Third-Party Discovery

In addition to the statutory grant of discovery authority against parties in vaccine compensation claims, the U.S. Court of Federal Claims, and the Office of Special Masters have the authority to conduct discovery involving non-parties.

The Court may issue a subpoena requiring any person to "attend and give testimony or to produce and permit inspection and copying of designated books, documents or tangible things," and the subpoena "may be joined with a command to appear at trial or hearing or deposition."

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RCFC 45(a)(1)(D). The subpoena power of the Court is not limited to parties; in fact, the rules specifically describe the limits on subpoenas directed to non-parties. RCFC 45(c). Third-party subpoenas are authorized subject to the protections described at RCFC 45(c)(1) and (2), and non-parties are provided the right to move to quash or modify a subpoena. RCFC 45(c)(3). The scope of discovery within the subpoena power of the Court under RCFC 45—whether of parties or non-parties—is generally described and limited by RCFC 26. *Capital Properties, Inc. v. The United States,* 49 Fed.Cl. 607, 611 (2001) (discovery against non-parties must meet "good cause" standard under RCFC 26(c)).

Court of Claims cases have authorized several forms of discovery against non-parties. In *Capital Properties, supra*, the Court allowed plaintiff to take the pre-trial deposition of a non-party (a representative of the state of Rhode Island), required Rhode Island to produce relevant documents, and required Amtrak (also a non-party) to produce documents. Extensive document production was ordered by the Court against a corporation that was not a party to litigation between an Indian tribe and the United States. *Navajo Nation v. The United States,* 46 Fed.Cl. 353 (2000). The Court permitted discovery of proprietary business information in *Levine v. The United States,* 226 Ct.Cl. 701 (1981). In all of these cases the Court ordered some form of the various discovery devices generally permitted under RCFC 27 – 36, subject to the scope and limitations of RCFC 26.

The rules and relevant cases make it clear that the Court of Claims is authorized to compel discovery from non-parties, giving rise to the question of whether the Special Master has such authority, because the terms "the Court" and "the Special Master" are *not* synonymous. In this case, however, the discovery power of "the Court" and "the Special Master" *are* synonymous, as the Vaccine Rules specifically give the Special Master discovery authority essentially concurrent with that of the Court of Claims.

Under Vaccine Rule 7, there is no discovery as a matter of right in Vaccine Court proceedings. The rule is consistent with the language of the Vaccine Act allowing only such

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discovery as "required by the special master," rather than discovery as a matter of right in civil litigation under the federal or state rules of procedure. 42 U.S.C. 300aa-12(d)(3)(B). The statute also explicitly allows the Special Master to "require such evidence as may be reasonable and necessary" and to " require the testimony of *any person* and the production of *any documents* as may be reasonable and necessary." 42 U.S.C. 300aa-12(d)(3)(B)(i), (iii) (emphasis added). Congress, by giving the Special Master the authority to conduct discovery as to "any" people and "any" documents, expressly allowed the Special Master to conduct discovery not limited to the parties in a compensation proceeding. The rules of the Vaccine Court, promulgated under 42 USC 300aa-12(d)(2), therefore specifically allow the Special Master to require third-party discovery.

The Vaccine Rules grant the Special Master the authority to conduct any of the discovery that is within the power of the Court of Claims under the RCFC. VR 7(b) (authorizing the use of the "discovery procedures provided by RCFC 26-37" in proceedings before the Special Masters). The rules specifically authorize the Special Master to issue subpoenas pursuant to RCFC 45. VR 7(c). Vaccine Rule 7 therefore incorporates the discovery and subpoena rules of the Court of Claims, giving the Special Master discretion to conduct discovery as permitted under RCFC 26-37 and RCFC 45. Since the rules of the Court of Claims and the relevant case law authorize the Court to require discovery from non-parties, and the Special Master has the discretion to utilize all of the discovery power provided to the Court, the Special Master has the authority to conduct discovery involving non-parties.

C. The Requested Discovery is Reasonable and Necessary to the Just Resolution of General Causation Issues in the Omnibus Proceeding

1. The VSD Provides Essential Information about Vaccine Safety, Information not Available Through Other Means.

That the requested access to the VSD is reasonable and necessary to the Special Master's resolution of general causation issues in the Omnibus Proceeding has been the subject of earlier briefing, and of expert witness testimony. Rather than restating those arguments yet again, and

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in the interest of economy, petitioners direct the Special Master to the following record already developed on this issue:

1. "Petitioners' Motion to Compel Discovery in the Autism Omnibus Proceeding," Motion at 5(b) and 5(c); pages 19-21;

2. "Petitioners Reply in Support of Motion to Compel Discovery," pages 11-14;

3. Testimony of Harland Austin, Ph.D., September 29, 2004.

Petitioners and their experts, however, are not the only voices recognizing the importance of VSD-based population studies to any inquiry examining a potential association between vaccine exposure and adverse health outcomes. As described in 2005 by the Institute of Medicine, the VSD is a unique and powerful research tool:

> The VSD is a unique national resource for evaluating vaccine safety. It includes data from administrative records for more than 7 million members of eight MCOs (Davis, 2004). The VSD database links data on patient characteristics, health outcomes (according to data resulting from inpatient, outpatient, and emergency room records), and vaccination history (vaccine type, date of vaccination, manufacturer, lot number, and injection site) (Davis, 2004). The VSD is a valuable tool for the retrospective assessment of vaccine safety because the number of people included is large, they generally receive most of their health services at the MCOs, and demographic, health outcome, and vaccination data are maintained electronically.[3]

The IOM further describes the VSD as a tool specifically created to overcome the limitations of other data storage and retrieval methods used to monitor vaccine safety, such as the "Vaccine Adverse Event Reporting System" (VAERS).[4] The unique characteristics of the VSD—the number of children enrolled, the time period for which data is available, the level of detail about the vaccines administered, and the ability to link these and other variables in a large population—make the VSD a "robust database for large retrospective studies" of the sort proposed by petitioners here, and is "a valuable resource for a variety of studies."[5]

The importance of the VSD and the critical need for easy access to VSD data is described by the IOM:

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[3] "Vaccine Safety Research, Data Access, and Public Trust," Institute of Medicine, National Academy of Sciences, (December 2005), p. 1. The full text of the IOM 2005 Report is Attached as Exhibit 87.
[4] *Id.*, at 27.
[5] *Id.*, at 30.

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> The value of the VSD data sharing program will be enhanced by easy access to the data, so that a variety of researchers can conduct a range of studies and have their findings reviewed by peers and discussed in ways conducive to the advancement of knowledge about vaccine safety. The VSD is a valuable resource for the nation. Efforts should be made to facilitate access to VSD data and their appropriate utilization, while protecting the confidentiality of information contained therein. Ensuring the independence, transparency, and fairness of VSD research activities is important for ensuring public trust in the VSD as a tool for addressing critical vaccine safety questions.[6]

2. DHHS Itself Recognizes the Value of a Study Such as that Proposed by this Motion.

It should be emphasized that petitioners do not seek unlimited or open-ended access to the VSD—this is hardly a "fishing expedition." Instead, petitioners seek access to the VSD that will allow a team of highly qualified investigators to conduct a specific study explicitly designed to directly address the central causation questions presented in the Omnibus Proceeding. The proposed retrospective cohort population study is similar in basic design to the smaller, more limited, and more time-bound VSD population study investigating possible associations between thimerosal exposure and neurological disorders conducted by a team of CDC researchers led by Dr. Thomas Verstraeten, published in November 2003.[7] The limitations of that study have been detailed in petitioners' earlier submissions and were the bases for the Special Master's "Discovery Order" of April 14, 2005 allowing petitioners' experts to conduct a limited "reanalysis" of the published article. The need for an expanded study examining the potential association between thimerosal exposure and neurological and neurodevelopmental injuries is articulated by the National Institutes of Health and the National Institute of Environmental Health Sciences of the U.S. Department of Health and Human Services in a report released in late October 2006, attached as Exhibit 88.[8]

In assessing various potential research uses of the VSD as a tool to investigate vaccine safety, the report favorably describes an "expansion of the VSD study published by

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[6] *Id.*, at 7-8.

[7] Verstraeten, T., et al, "Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized Health Maintenance Organization Databases," *Pediatrics,* 112(5):1039-1048 (November 2003). See Petitioners Ex. 22.

[8] "Report: Thimerosal Exposure in Pediatric Vaccines," National Institutes of Health, of the Department of Health and Human Services, October 2006.

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Verstraeten."[9] Specifically, the report recognizes the value of a retrospective cohort study "that would include additional years for follow up, would add more MCOs and reexamine the criteria for exclusion of births, or take a sensitivity approach to examining the impact of various exclusion criteria."[10] ***This is almost exactly what petitioners' proposed study seeks to accomplish.***

In short, the IOM, NIH, NIEHS and DHHS all agree that the VSD is a powerful tool that is uniquely suited to generating analyses that would assist the Special Master's inquiry into the question of whether there is an association between thimerosal exposure and neurological or neurodevelopmental injuries that might be established in a population study. All of these government policy and research entities recognize the shortcomings of the one relevant VSD study to date. The NIH, NIEHS and DHHS have now reported that a large, VSD-based, retrospective cohort study such as that proposed by the PSC should be strongly considered as a way to determine if there is an association between thimerosal exposure and adverse health outcomes. It is no longer just the petitioners arguing that such a study is reasonable and necessary—respondents' own client agencies have now finally joined the chorus.

Petitioners note that supportive epidemiology is *not* a required element of proving causation in the NVICP, and the petitioners could very well establish general and individual causation in these Omnibus claims without epidemiological evidence. To the extent that the Special Master will consider epidemiology in his causation inquiry at all, however, he should find that allowing the VSD study proposed by the PSC in this Motion is reasonably necessary to resolving any general causation issues that turn on population studies. The instant Motion should be granted so that the study can begin.

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[9] *Id.*, at 7.
[10] *Id.*, at 8.

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D. The CDC Continues to Exercise Control Over the VSD, and Controls Access to the VSD

Beginning in January 2001, the CDC transferred administrative oversight of the VSD to a third-party vendor, America's Health Insurance Plans (AHIP), the national trade association for managed care organizations (MCOs). As part of the contract with AHIP, the CDC no longer maintains an archive of VSD data generated after December 2000 and automated VSD output is no longer collected by the CDC. Data generated after December 2000 are not available to external researchers through the CDC's Data Sharing Guidelines.

The CDC's decision to privatize management of the VSD created serious obstacles to external researchers attempting to conduct studies using the VSD, generated confusion within the scientific community about access to the VSD, sowed doubts as to the type and quality of VSD data available, and undermined public trust in the nation's vaccine safety program, all as described by the IOM's 2005 Report. The CDC management contract with AHIP also raised questions about the various roles of the federal government, the individual MCOs, and AHIP in collecting, managing, and analyzing VSD data. The 2005 IOM report specifically addressed questions about VSD access and the ability of external researchers to conduct investigations using the VSD.

In addition to the IOM's inquiries, private litigants have used the civil discovery process in at least one US District Court to address VSD access and control issues with AHIP itself. The plaintiffs in a lawsuit filed in the US District Court for the Eastern District of Pennsylvania (*Sykes v. Glaxo-SmithKline, et al.*, Case No. 06-CV-1111) sought the third-party deposition of Barbara Lardy, AHIP's VSD project manager. Ms. Lardy testified, among other things, about the CDC's ongoing involvement with the VSD, particularly the CDC's involvement in regulating access to VSD data by external researchers.

The IOM report and Ms. Lardy's testimony make it clear that despite "outsourcing" the management of VSD data, particularly post-December 2000 data, the CDC continues to exercise significant control over access to the VSD, and the CDC itself has access to the VSD not

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available to external researchers. Specifically, the CDC controls access to the VSD in the following ways:

1. CDC receives monthly activity reports on VSD activity from each of the MCOs participating in the VSD;[11]

2. CDC receives regular reports and updates on ongoing studies in the VSD;[12]

3. Completed data files generated by ongoing VSD studies are collected regularly by the CDC from the MCOs whose data is being used in an ongoing study;[13]

4. The CDC has access to formatted data files generated by the VSD database, and access to data files is provided to the CDC on a regular schedule;[14]

5. CDC decides what VSD studies ought to be conducted, and sets priorities among the VSD studies to be conducted;[15]

6. CDC researchers have opportunities to propose VSD studies, opportunities specifically not granted to external researchers;[16]

7. The CDC excludes external researchers from accessing VSD data, participating in study designs, and setting VSD research priorities;[17]

8. The CDC requires that external researchers collaborate with a CDC investigator in order to conduct VSD research, and the ability of any external researcher to access the VSD is controlled by the CDC's willingness—or unwillingness—to provide an internal, collaborative investigator for that external researcher;[18]

9. The CDC controls and limits the ability of external researchers to access, "audit," or reanalyze ongoing or completed VSD studies by withholding from external researchers all

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[11] *Sykes,* Barbara Lardy Deposition, p. 61:4-8. Deposition excerpts attached as Exhibit 89.
[12] *Id.,* p. 62:10 – 64:7
[13] *Id.,* p. 65:5-16
[14] *Id.,* p. 67:13 – 68:19
[15] *Id.,* p. 86:17 – 87:10
[16] IOM 2005 Report, p. 82
[17] *Id.,* p. 80
[18] *Id.,* pp. 61-63

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datasets, data files, data analyses, study designs, exclusion/inclusion criteria, and programming queries *except* for final datasets.[19]

10. Internal CDC researchers are conducting ongoing studies that rely on access to the VSD, including post-2000 VSD data, access not available to external researchers.[20]

There can be little doubt that the CDC has a virtual monopoly on VSD access not available to external researchers, and that the CDC completely controls who may access the VSD. The CDC describes the VSD project as a "data sharing program," but the CDC policies that essentially cut-off access to the VSD by external researchers mean that the program fails to meet the scientific standards for "data sharing." As described by the IOM in 2005:

> If the current limitations of the program are not overcome, the NIP [National Immunization Program] should characterize the program as a limited data access program rather than a data sharing program.
>
> A true VSD data sharing program would need to include the following three elements: access to the core VSD for exploratory analyses; access to studies that involve chart review, and so on, to consider alternative explanations; and new collaborative studies with the NIP and the MCOs to pursue new hypotheses. ***If the intention is to allow true data sharing, researchers should be allowed use of all available years of data for new studies and not be limited to final datasets for reanalyses.***[21] (emphasis added).

Because of the virtually complete control exercised by the CDC over access to the VSD, the CDC is properly subject to an Order of the Special Master directing the CDC (and its appropriate subdivisions such as the Research Data Center and the Immunization Safety Office) to provide access to the VSD for the specific, limited purpose of the petitioners' proposed study.

E. The MCOs Participating In The VSD Have Possession And Control Of The Relevant Data

The MCOs participating in the VSD have always, and still are, the source of all data in the VSD. From the beginning of the VSD project in the early 1990s until the CDC outsourced management of the VSD by contract with AHIP in September 2002, the automated datafiles

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[19] *Id.*, pp. 63-65

[20] Presentation at the National Vaccine Advisory Commission meeting, October 11, 2006, by Dr. Tanja Popovic, Associate Director for Science, CDC, p. 4; attached as Exhibit 90.

[21] "Vaccine Safety Research, Data Access, and Public Trust," Institute of Medicine, National Academy of Sciences, (December 2005), p. 36; attached as Exhibit 87.

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containing VSD data were delivered to the CDC by the MCOs. The datafiles containing VSD data through the end of December 2000 were "maintained at CDC and considered a database owned by CDC."[22] All post-2000 data generated by the VSD, however, is no longer delivered to the CDC, and instead remains with the MCOs and is considered to be owned by the MCOs.[23]

Each of the MCOs maintains several administrative databases that track, among other things, the ongoing medical histories of MCO member patients, as well as the vaccine histories of the members. The MCOs then extract relevant information from those databases into a consolidated form—the VSD—that allows medical histories and vaccine exposures to be linked in multiple ways.[24] The MCOs update the VSD annually.[25] The MCOs generate the data upon which the VSD is based, they organize and consolidate the data to create the VSD, they review the data for accuracy and completeness, they develop protocols to make data entries consistent over time, they update the VSD annually, and they retain both the "source" data and any datafiles generated by the VSD.

There is no doubt, therefore, that the MCOs have both possession and control of the VSD, and specifically of the post-2000 data that is the subject of petitioners' Motion. As entities in possession and control of the VSD, the MCOs are proper subjects of a subpoena from the Special Master directing the MCOs to provide the relevant datafiles.

F. Petitioners' Motion, in the Alternative, to Exclude Respondent's Evidence Relying on the VSD

Petitioners obviously believe that VSD access that meets scientific standards for data sharing is critical to the Special Master's general causation inquiry, to the extent that the inquiry will rely in part on population or ecological studies. VSD access of the sort requested by the PSC is also critical to addressing broader vaccine policy issues: the integrity of the immunization program, public trust in the government's immunization safety oversight, and transparency in

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[22] *Id.*, p. 29
[23] *Id.*
[24] *Id.*
[25] *Id.*

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science and policy-making. It is for all of these reasons that petitioners have for the past three years vigorously sought access to the VSD.

If, however, the Special Master denies the instant Motion, petitioners move in the alternative for an Order excluding any evidence proffered by respondent that relies in whole or in part on the VSD. The rationale is simple and based on fairness. Respondent cannot be allowed to monopolize control over the creation and access of evidence in support of its case, while simultaneously denying petitioners any access to the same evidence. This is particularly so in an instance where the evidence—the VSD—is a public resource, publicly funded, and intended to serve the public's interest in vaccine safety and efficacy.

The PSC defers briefing this alternative motion to exclude at this point because it is not ripe; that is, the Special Master has not ruled on the Motion to Compel. The PSC of course trusts that the alternative motion will be moot upon the Special Master's allowance of the Motion to Compel or a decision to issue subpoenas to the MCOs.

G. Conclusion

For all of the reasons described above, the Special Master should allow this Motion to Compel and order respondent to give petitioners and petitioners' experts access to the Vaccine Safety Datalink (VSD) for purposes of an investigation into potential associations between thimerosal and MMR exposure and adverse neurological or developmental outcomes in children. In addition to such an Order, the Special Master should issue subpoenas to all participants in the VSD program, including the MCOs and any contractors with custody of the data in issue, requiring those third parties to give petitioners' and petitioners' experts access to the Vaccine Safety Datalink (VSD) for purposes of an investigation into potential associations between thimerosal and MMR exposure and adverse neurological or developmental outcomes in children.

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DATED this 7th day of December, 2006

WILLIAMS LOVE O'LEARY CRAINE & POWERS P.C.

By: _____

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CERTIFICATE OF SERVICE

I hereby certify that on December 7 2006, I served the foregoing **PSC SECOND MOTION TO COMPEL VSD ACCESS** on the following individual(s):

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PLAN TO INVESTIGATE POTENTIAL VACCINE RISK FACTORS FOR AUTISM AND OTHER NEUROLOGICAL AND NEURODEVELOPMENTAL DISORDERS, USING THE VACCINE SAFETY DATALINK

1. Introduction

There are a number of critical issues relating to potential causes of the epidemic increase of autism in the United States. We understand that there is a large reservoir of data available that may provide useful information important for patients and the medical community.

We, a group of academic physicians and scientists, were recruited by the Petitioners Steering Committee (PSC), attorneys appointed by the US Court of Federal Claims to represent the children and their families who have made claims for compensation due to autism or other developmental disorders related to the children's exposure to organic ethylmercury from thimerosal in infant vaccines, or from exposure to the MMR vaccine, or from a combination of thimerosal and MMR exposures, in the USA. We were asked to assume that the PSC's retained experts would be given access to data from the Vaccine Safety Datalink (VSD) database, and to design a protocol for a reasonable set of analytic studies to investigate possible associations between thimerosal exposure, MMR exposure, and adverse outcomes in the VSD.

We note that a special advisory committee set up by the Institute of Medicine, the Committee on the Review of the National Immunization Program's (NIP) Research Procedures and Data Sharing Program, in its official report published in 2005,[1] made several specific recommendations to be implemented by the NIP to facilitate exactly such studies of the VSD data as are proposed here.

2. Hypotheses and goals

Our goal is to test the issue of causation and address it through rigorous analysis of associations in the data.

The primary null hypothesis for the proposed study is that there is no association between the amounts of thimerosal or MMR vaccines that an infant received *in utero* or in the first two years of life and neurodevelopmental outcomes such as autism or autism spectrum disorder symptoms.

Because it is plausible that organic mercury could interfere with the development of an infant's immune system, and it is also plausible that live measles virus particles could cause immune system malfunction, there is a secondary null hypothesis that there would be no association between outcomes symptomatic of immunologic pathology and the amount of thimerosal or MMR vaccines to which each child was exposed.

Because it is plausible that organic mercury could interfere with the neurological functioning of the developing cardiovascular system, there is another secondary null hypothesis that there

[1] "Vaccine Safety Research, Data Access, and Public Trust, " Institute of Medicine 2005, National Academy Press.

would be no association between outcomes of cardiovascular diseases, such as arrhythmias, and the amount of thimerosal or MMR vaccines to which each child was exposed.

The study outlined here will examine these causal hypotheses by analyzing the associations of thimerosal with adverse outcomes after adjustment for potentially biasing factors. In all cases the alternative hypothesis is that there is a positive association (a one-sided alternative).

3. Brief description of the VSD

As of December 31, 2001, there were nearly 2,000,000 children (age<18) enrolled at eight participating managed care organizations (MCOs), representing 2.7% of the US population. By the end of 2004, there were almost 2,300,000 children under age 18 enrolled in participating MCOs.[2]

In order to maintain HIPAA required confidentiality, the VSD moved to a distributed data model in 2001, allowing full VSD datasets to remain at the MCO sites rather than being transferred to the CDC, but with an established method to access the VSD data through SAS programs submitted to the MCO by researchers.

4. Scope of data needed for these studies

In order to carry out the analyses proposed here, the investigators will need access to thimerosal and MMR exposure data for all children born into VSD participant MCOs from January 1992 through December 2004, or later if the data is available; this requires cross-linking of all vaccines administered to each child in the study, with sufficient information about the type and source of each vaccine to determine its thimerosal content, similar to the data provided to Dr. Thomas Verstraeten for his study published in Pediatrics in 2003.[3]

Dr. Verstraeten's study assumed that all vaccines included in the analysis came from multi-dose vials with thimerosal used as a preservative,[4] but there were some thimerosal-free DTaP vaccines available to physicians beginning in the 1990's. It is important to be able to access the data on those patients who received this special type of DTaP vaccine.

The proposed study will also need data about thimerosal content for each lot of vaccine from 1999 onwards, and, in particular, the date that they became thimerosal-free.

The proposed study will further require data for the diagnostic outcome for each ICD code for all children in the CMOs, including patients in both clinics and in hospital, from 1992 onward. We note that this request is important because in the study by Thomas Verstraeten, speech and language disorders were not consistently coded between CMOs.[5]

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[2] "Use of the Vaccine Safety Datalink to Assess Time Trends in Autism: Feasibility and Study Design Considerations", Conference Presentation, NIEHS and CDC Joint Conference (May 4, 2006).
[3] Verstraeten, T., et al. *Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized HMO Databases*, Volume 112, No. 5 PEDIATRICS, 1039 (November 2003).
[4] *Id.*, at p. 1040.
[5] *Id.*

If available, the investigators will also need cross-linking data that will reflect all immunoglobulin vaccines or injections administered to the pregnant mothers of the children in the study. This is required for us to determine the input of *in utero* exposure to thimerosal.

All of these data sets must be compatible with pooling of the analysis across CMO's.

5. **Anticipated subgroup analyses**.

Our anticipated subgroup analyses will include the following groups:

1. Stratification of results by CMO.
2. Stratification of thimerosal dose into categories that are internally similar, followed by comparison of risk in all categories to lowest, and also to the group of children with no exposure.
3. Trend analysis using statistical models for the relation of thimerosal dose to outcome risk.
4. Stratification of results according to low birth weight.

6. **Statistical methodology**

1. In addition to basic categorical analyses, in order to avoid artifacts due to inappropriate grouping of exposures or from residual confounding due to categorizing covariates, we will also use flexible trend models with adjustment for possible confounding factors, for example logistic regression with fractional polynomials or splines.

2. In order to detect possible artifactual (spurious) associations arising from the multiple comparisons being made, we will repeat analyses using multilevel methods (also known as hierarchical, random-coefficient, or shrinkage methods) to regress estimates toward values expected from null models.

3. We will use proportional hazard models to estimate RR's at each MCO, stratified by sex, and year and month of birth and clinic most often visited.

4. Verstraeten was concerned regarding screening bias for health seeking behavior (those children with vaccinations on time tended to have more well baby visits for many purposes, and thus more likely to be diagnosed with something). We will include variables that include this information for adjustment purposes.

5. We will model exposure as both a continuous and categorical variable.

6. Possible exclusionary criteria:

a. Verstraeten excluded all children who did not have at least two polio vaccinations by age of 1 as surrogate for children who might not be receiving most of their care thru the HMO.[6]

b. Verstraeten also excluded extremely low birth weight children (<2500g) and children with congenital or severe perinatal disorder. Verstraeten separately analyzed birth weight children between 1500 and 2499 g).[7]

c. Verstraeten also restricted analsyses to children who were continuously enrolled at the HMO for the first year of life.[8]

This proposed analysis will experiment with exclusion effects but we will not force them into sampling, as was done by Verstraeten, as these can produce an irremediable bias in the sample. This inclusion will also allow us to examine the effects of exclusions.

We cite the following work to illustrate our methodology:

Greenland, S. (1995). Dose-response and trend analysis: Alternatives to category-indicator regression. *Epidemiology*, 6, 356-365

Greenland, S. (2000). Principles of multilevel modelling. *International Journal of Epidemiology*, 29, 158-167.

Greenland, S. (2000). When should epidemiologic regressions use random coefficients? *Biometrics*, 56, 915-921.

Hernán MA, Hernandez-Diaz S, Robins JM (2004). A structural approach to selection bias. *Epidemiology*, 15, 615-625.

7. List of ICD codes for analysis:

The VSD uses the ICD-9 system to code outcomes. Verstraeten used the following ICD-9 categories:[9]

299. Infantile autism
299.8 Other childhood pyschosis
307.0 Stammering
307.2 Tics
307.4 Sleep disorders
327.3 Circadian rhythm sleep disorder
307.5 Eating disorders
313.8 Emotional disturbances

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[6] *Id.*
[7] *Id.*, and Appendix 1.
[8] *Id.*, at 1040.
[9] *Id.*, at 1042.

314.0 ADD
315.31 Developmental language delay
315.39 Developmental speech delay
315. 3 Speech or language delay
315.4 Coordination disorder
357 Inflammatory and toxic neuropathy
728.87 Muscle weakness (generalized)

For immune disorders, we need the VSD outcome data for:

279 Disorders involving the immune mechanism
279.4 Autoimmune disease, not elsewhere classified

For cardiovascular disorders, as suggested by Dr. Grandjean's studies of Faroe Islands children exposed to organic mercury in utero:[10]

401 Essential hypertension
402 Hypertensive heart disease
403 Hypertensive renal disease
404 Hypertensive heart and renal disease
425 Cardio myopathy
427 Cardiac dysrhythmias
427.1 Paroxysmal ventricular tachycardia
426.82 Long QT syndrome
427.41 Ventricular fibrillation
427.69 Other (Ventricular premature beats, contractions, or systoles
427.0 Paroxysmal supraventricular tachycardia
428 Heart failure
429 Ill-defined conditions and complications of heart disease
746 Other congenital anomalies of the heart
785 Tachycardia, unspecified (and other)
275 Disorders of metal metabolism
277.1 Disorders of porphyrin metabolism
779.82 Neonatal tachycardia

[10] Grandjean, P., et al. *Cardiac Autonomic Activity in Methylmercury Neurotoxicity: 14-year Follow-up of a Faroese Birth Cohort*, J PEDIATR. 2004 Feb; 144(2):169-76; and Sorensen, N. et al. *Prenatal Methylmercury Exposure as a Cardiovascular Risk Factor at Seven Years of Age,* EPIDEMIOLOGY, 1999 Jul; 10(4):370-5

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Petitioners' Exhibit 87

The text of this Exhibit has been made part of the Autism Master File, but it has not been placed on this website because it is a copyrighted publication. The citation for this item is:

Institute of Medicine, "VACCINE SAFETY RESEARCH, DATA ACCESS, AND PUBLIC TRUST" (National Academies Press, 2005)

Petitioners' Exhibit 88

The text of this Exhibit has been made part of the Autism Master File, but it has not been placed on this website because it is a copyrighted publication. The citation for this item is:

National Institutes of Health, of the U.S. Department of Health and Human Services, *Thimerosal Exposure in Pediatric Vaccines: Feasibility of Studies Using the Vaccine Safety Datalink* (October, 2006).

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

LISA SYKES and SETH SYKES, Individually and as Parents and Natural Guardians of WESLEY ALEXANDER SYKES, a minor child, Plaintiffs,	:	
v.	:	CASE No.
GLAXO-SMITHKLINE, Individually and as successor-in-interest to Smith Kline Beecham Corporation; WYETH, Inc., f/k/a AMERICAN HOME HOME PRODUCTS CORPORATION, d/b/a WYETH, INC., WYETH LABORATORIES, WYETH-AYERST, WYETH-AYERST, LABORATORIES, WYETH LEDERLE, WYETH LEDERLE VACCINES, and LEDERLE LABORATORIES, and BAYER PHARMACEUTICALS CORPORATION, f/k/a Bayer Corporation, Individually and as Successor-In-Interest to Miles, Inc., Defendants.	:	06-CV-1111

30(b)6 DEPOSITION OF America's Health Insurance Plans BY AND THROUGH ITS DESIGNEE

BARBARA LARDY
Washington, D.C.
Tuesday, October 10, 2006
10:14 a.m.

Job No.: 176897
Pages 1 -
Reported by: Tristan-Joseph, RPR

CERTIFIED COPY

EXHIBIT 89
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included in their Monthly Activity Report?
A. No.
Q. That would be a separate thing that they would deliver to AHIP?
A. Yes.
Q. And based on those invoices, AHIP would compile those and sent a quarterly report to the CDC; is that right?
A. That's right.
Q. Okay. Then in Item No. 3 it says Conference Call Minutes.
What conference calls are being described here in this deliverable item?
A. It's not specified which conference calls we -- in -- I mean, this, what you see is what it is. In practice, we do minutes on the -- primarily the monthly network call and then the working group calls that go on throughout the minutes so.
Q. Would any of the conference calls be discussing ongoing studies in progress that are using the VSD as a resource?

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MR. HOLLOWAY: Object to the form of the question.
THE WITNESS: The minutes would -- as I think when you were talking earlier about minutes, the minutes would talk about the tracking or the stage of the study. It would not -- there's no data revealed in the minutes.
BY MR. POWERS:
Q. So no data revealed. Would it be fair to say that no substantive discussion about the scientific work is discussed during these conference calls?
A. Well, the -- they would talk about what -- on a conference call we talk about what the goal of the study was, which sites were participating, what, you know, what the elements were that they were looking at. So to the extent -- I don't know if that's getting at what you're asking.
Q. Right.
A. But there's no -- there's no data that's discussed in the calls.

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Q. Okay. And then for item -- oh, I'm sorry. Then the conference call minutes, these are calls that AHIP coordinates. Correct?
A. Yes.
Q. And then AHIP compiles these minutes and sends them periodically to the CDC?
A. Yes, on the schedule specified here.
Q. Right. And then on Item No. 4, it says, "Reports on data collection procedures, numbers and results of validation procedures performed."
Who is delivering that particular item to the CDC?
A. That's provided by the sites, by the research -- the participating HMOs.
Q. Now do the HMOs send, this deliverable Item No. 4, do they send it directly to the CDC?
A. Yes.
Q. Do they send a copy to AHIP also?
A. No.
Q. So does AHIP ever see the reports on data collection as described in Item No. 4?
A. No.

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Q. Does CDC ever send copies of those reports back to AHIP after receiving them from the HMOs?
A. No.
Q. Does AHIP have any record on what -- understanding that your testimony is they don't have the reports themselves, does AHIP have any record of what reports the individual sites would have sent to the CDC?
MR. THOMASCH: Objection to form.
THE WITNESS: The only thing that the sites would say in their monthly report to us would be, you know, completed data files and sent to the CDC. That would be the extent. It would just be, you know, that they were meeting the deliverable specified here.
BY MR. POWERS:
Q. Okay. But they wouldn't send you a copy of a deliverable --
A. No.
Q. -- in Item No. 4?
Okay. Again, Item No. 5, Access to

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provisional limited data files, who provides that deliverable in Item No. 5 to the CDC?
A. That's the sites, the research sites.
Q. Do the research sites send Item No. 5 to AHIP and in addition to sending it to the CDC?
A. No.
Q. Does AHIP get a copy of Item No. 5 from the CDC after it's been delivered to the CDC?
A. No.
Q. Does AHIP, from any source, get a copy of Item No. 5 as described in this schedule?
A. No.
This is also a mistake in the contract because it says, "Starting 180 months after contract award."
Q. Yeah, the contract would have been long gone before you first had to deliver that.
I was going to ask about that.
Is it days?
A. I --
Q. Should it be days rather than months --
A. I believe --

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Q. -- if you know?
A. I believe it should be days.
Q. One would assume, but okay.
Now understanding that your testimony is that AHIP doesn't get Item No. 5 at any point, does AHIP receive designated database files in SAS format through any other means other than Item No. 5?
A. No.
MR. HOLLOWAY: Object to the form of the question.
BY MR. POWERS:
Q. Now in Item No. 6, it is described here as Access the data files, containing the designated database files with appropriate format.
Who is responsible for delivering that item to the CDC under the contract?
A. As with the two previous, it is the sites that are responsible for that. And it's listed on the delivery schedule because access is what's being delivered.
Q. And I'm going to ask some of the same

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questions then.
The access is what's being delivered and it's the -- the individual sites are delivering access to the CDC; is that correct?
A. Yes.
Q. Does AHIP ever have access to data files as described in Item No. 6?
A. No.
Q. Does AHIP have access to any designated database files as described in Item No. 6?
A. No.
Q. Aside from delivery to the CDC, are you aware of any other entities to whom Item No. 6 might be delivered pursuant to this contract?
MR. THOMASCH: Objection to form.
MR. HOLLOWAY: Calls for speculation.
THE WITNESS: It's specified that it goes to the CDC so that's basically what happens, to my knowledge.
BY MR. POWERS:
Q. Okay. And then Item No. 7, there's a draft annual report containing information as set

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feather in the SOW.
Now SOW, is that Scope Of Work?
A. Yes.
Q. Okay. Who's responsible for delivering that to the CDC?
A. AHIP delivers that to the CDC.
Q. And then Item No. 8, the annual report, this would be, I guess, the final version of what was described as a draft to No. 7?
A. Yes.
Q. That annual report, AHIP would deliver that to the CDC?
A. Yes.
(Whereupon, Mr. Shoemaker briefly confers with Mr. Powers.)
BY MR. POWERS:
Q. Okay. I'm done with page 11.
If you want to turn to page 25. And again, at the top, right-hand corners it's marked page 25 of 38.
Let's go ahead and find that page and then look up so that I know that you are on the

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listed that would be participating that are not included?
A. No.
Q. Now this annual report talks about priority studies.
You'll have to flip back to page 5, which is the table of contents.
Do you see -- it's one, two, like the fourth item down on the Table of Contents where it says VSD Priority Studies.
A. Mm-hmm.
Q. Do you see that?
Then there's a list of studies under there. It looks like there's one, two, three, ten studies; is that correct?
A. Uh, yes.
Q. What makes a particular study a priority study?
A. As we were discussing before, every year the CDC and the principal investigators review emerging vaccines, what, you know, what issues are out there, and they decide on a list of studies

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that they believe are most important and that need to in terms of having some priority in terms of finishing them up.
Q. So does AHIP participate in prioritizing among the different studies that are underway?
A. No.
Q. And who, again, makes those priority decisions?
A. It's made by the CDC and by the scientific investigators at the sites.
Q. At the sites, okay.
There are these 10 priority studies listed in the 2003 report.
Are you aware of any other studies that were going on, in addition to these list of priority studies, at the time the 2003 report was published?
A. I can't give you a list off the top of my head but, as a general rule, there are probably -- at all the sites combined there are probably between 50 and 60 studies at some stage of development at any one time, so yes.

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Q. So it's from within that pool of studies going on at the various sites that a priority list is generated; is that fair?
A. Yes.
Q. Okay. Since the 2003 report has come out has this priority list changed as far as you know?
In other words, have any studies come off the list?
Have any studies come on to the list?
A. There are -- there have been studies that have been added.
Q. And to the --
A. And --
Q. I'm sorry.
A. And a number of these are close to conclusion. A number are still in the data collection phase. And the rapid cycle --
Q. Mm-hmm.
A. -- study that's listed --
Q. Yeah, that would be number nine, the Rapid Cycle Analysis?

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A. Yes.
Their -- rapid cycle is -- it's not just one study. They're increasing more rapid cycle. The idea is to have the data more up-to-date and to get some information more quickly than the cycle data sets in the past.
Q. Okay. And to the extent that you know, could you identify any studies since 2003 that would be described as a priority study by AHIP?
A. Just repeat that you're asking --
Q. Yeah.
A. -- addition -- additional studies?
Q. Right.
Just to the extent that you know, can you identify any priority studies in addition to the ones that we see here?
MR. THOMASCH: Objection to form.
THE WITNESS: Most of -- the studies that are on here, I think our -- the majority of them, there's one that I can recall that's being added for the new Menactra vaccine, a meningococcal vaccine, but that's the only one I can think of.

Immunization Safety Office (ISO) Overview

Robert L. Davis, MD, MPH
Director
Immunization Safety Office
Office of the Chief Science Officer
Centers for Disease Control and Prevention

CDC

Vision

- To perform surveillance and high-quality research for CDC vaccine safety activities, to identify adverse events after vaccination, to assess causality and preventable risk factors
- Communicate our findings in a clear and transparent manner so that:
  - partners can incorporate vaccine safety data into public health policy decisions
  - public can choose vaccination with confidence and with the least risk possible

CDC

Background

- In 2005, the Immunization Safety Office (ISO) was moved from the National Immunization Program to CDC's Office of the Director, Office of the Chief Science Officer (OCSO)
- This allowed CDC to meet its commitment to building a more robust vaccine safety activity able to keep pace with the increasing number and combinations of recommended immunizations

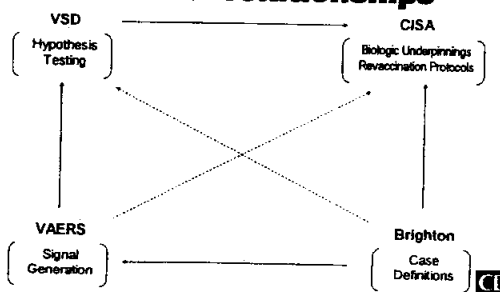
CDC

Background: ISO Key Components

- Vaccine Safety Datalink (VSD) project
  - 8 MCOs with comprehensive medical and immunization histories of over 5.5 million people, from a population of over 9 million people.
  - FY06 Funding Level:
- Vaccine Adverse Event Reporting System (VAERS)
  - Early-warning passive surveillance system to detect problems related to vaccines.
  - FY06 Funding Level:
- Clinical Immunization Safety Assessment (CISA) Network
  - In-depth clinical investigations of individuals with unusual or severe vaccine adverse events.
  - FY06 Funding Level:
- Brighton Collaboration
  - Global collaboration to standardize case definitions; provide common "vocabulary" for vaccine safety research.
  - FY06 Funding Level:

CDC

ISO Inter-relationships



CDC

Highlighted Achievements: Vaccine Adverse Events

Vaccine	Adverse Event	Public Health Impact
Rotavirus	Intussusception	Vaccine Withdrawal
DPT/MMR	Seizures	Clinical knowledge/VICP
Smallpox	General AE/myocarditis	Civilian vaccination program discontinued
Influenza (intranasal)	Bell's Palsy	Future vaccine development
MMR II	Arthralgia/Rash/Fever/Other	Policy change

CDC

Tanja Popovic, MD, PhD
Associate Director For Science, Centers for Disease Control and Prevention

Highlighted Achievements: Vaccine Safety

- No increased risk for multiple sclerosis after hepatitis B vaccination
- Increased safety profile of acellular pertussis vaccine compared with whole cell pertussis vaccine
- No increased risk for inflammatory bowel disease after MMR vaccine
- No increased risk for type 1 diabetes with routinely recommended childhood vaccines
- No increased risk for aseptic meningitis after MMR (Jeryl-Lynn) vaccine
- No increased risk for asthma after childhood vaccinations

CDC

Key Partners

- Public
- Providers
- State government, local government, and federal partners
  - FDA
  - NIH
- Vaccine manufacturers
- Scientists
- Other CDC CIOs

CDC

ISO Internal Peer Review
October 11, 2006

Vaccine Adverse Event Reporting System (VAERS)

Scott Campbell, MSPH
VAERS Team Lead
Immunization Safety Office
Office of the Chief Science Officer
Centers for Disease Control and Prevention

CDC

Mission

In partnership with the FDA, provide comprehensive post-marketing surveillance of all vaccine products licensed in the United States in a timely manner in order to protect all persons from unacceptable risks related to immunization

CDC

Background: The Solution

- VAERS established in1986 by the National Childhood Vaccine Injury Act
- First VAERS reports collected in November 1990
- Management / analysis of VAERS data shared between CDC and FDA

CDC

Goals

- Identify adverse events following immunization (AEFI) that were previously unrecognized
- Analyze trends of known AEFI
- Trigger clinical, epidemiologic, or laboratory investigations regarding causal/non-causal relationship between a vaccine or vaccine combinations and AEFI
- Provide information for setting public health policies on vaccine safety

CDC

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VAERS: Hypothesis Generation

CDC

Highlighted Achievement: Intussusception following RotaShield®

- VAERS published July 16, 1999 *MMWR* article identifying this AE among 15 recipients of RotaShield® vaccine
- VAERS reports triggered two large investigations by CDC and FDA, in collaboration with state and local health departments throughout the U.S.
- ACIP withdrew its recommendation to vaccinate infants with RotaShield® vaccine
- Manufacturer voluntarily withdrew RotaShield® from the market in October 1999

CDC

Long-term Plans

- Complete research on every newly-licensed vaccine
  - MMRV
  - MCV4
  - RTV
  - Varicella zoster
  - HPV4
  - Tdap (two formulations)
- Continue responding to public and partner inquires
  - 5 to 10 inquiries per week = 20 to 40 per month
  - 40 to 80 work-hours per month

CDC

The Vaccine Safety Datalink (VSD) Project

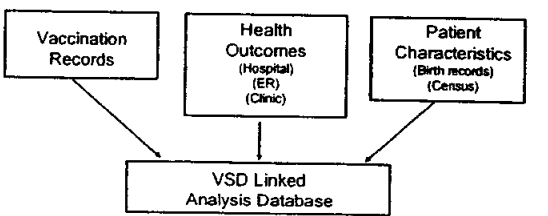
CDC

Vaccine Safety Datalink

- Began in 1991 as a collaborative project between CDC and four HMOs:
  - Group Health Cooperative, Seattle, WA
  - Northwest Kaiser Permanente, Portland, OR
  - Northern California Kaiser Permanente, Oakland
  - South California Kaiser Permanente, Los Angeles
- Expanded in 200 to include four more HMOs:
  - Harvard Pilgrim Health Care, Boston, MA
  - HealthPartners, Minneapolis, MN
  - Kaiser Permanente Colorado, Denver, CO
  - Marshfield Clinic, Marshfield, WI
- Total over 10 million members

CDC

VACCINE SAFETY DATALINK (VSD) Overview



CDC

EXHIBIT 90
PAGE 3 OF 5

VSD Study Types

- Screening analyses (automated data)
  - preliminary assessment of vaccine-outcome associations
- In-depth studies (chart reviews, interviews)
  - validate outcomes (and dates)
  - verify vaccination history (and dates)
  - additional risk factor or clinical information

CDC

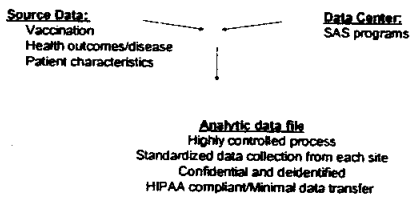
VSD Study Types

Example of in-depth evaluation studies

- Thimerosal exposure and risk for neurodevelopmental disorders
  - Cohort design based on exposure
  - Two day clinical evaluation of neurocognitive development
  - Extensive interview for covariate ascertainment
  - Extensive chart review for exposure (thimerosal) assessment
- Thimerosal exposure and risk for autism
  - Case-control design
  - One day clinical evaluation of cases (autism)
  - Extensive interview for covariate ascertainment
  - Extensive chart review for exposure (thimerosal) assessment

CDC

VSD Data management



CDC

ISO Internal Peer Review
October 11, 2006

Clinical Immunization Safety Assessment (CISA)

Claudia Vellozzi, MD, MPH
Logistics Health Incorporated
CISA Team Lead
Immunization Safety Office
Office of the Chief Science Officer
Centers for Disease Control and Prevention

CDC

Mission

- To conduct clinical research of immunization-associated adverse events (AE) and individual variation
- To provide evidence-based information that assists
  - clinicians in the evaluation and management of individuals at risk for AEFI
  - individuals to make informed immunization choices

CDC

Background

- Established in 2001 to investigate the pathophysiologic mechanisms and biologic risks of AEFI and to provide evidence-based vaccine safety assessments
- Network of six academic centers each with vaccine subject matter experts

CDC

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The CISA Network

- Boston Medical Center
- Columbia University Medical Center
- Johns Hopkins University
- Northern California Kaiser Permanente
- Stanford University Medical Center
- Vanderbilt University Medical Center

CDC

Priority Activities

Dedicate resources and focus towards priority investigations

- GBS following vaccination
  (CISA Goal: risk factors studies of AEFI using hypothesis-driven protocols)
- Hypersensitivity management
  (CISA Goal: develop evidence-based guidance for use by clinicians)
- Vaccination/Revaccination protocols
  - e.g. LVV in DiGeorge Syndrome
  (CISA Goal: develop evidence-based guidance for use by clinicians)

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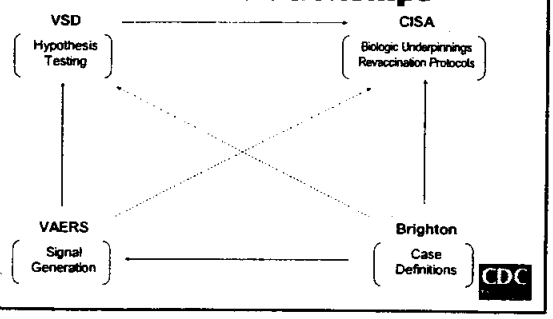
ISO Inter-relationships



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Challenges

- New vaccines
  - Rotavirus, Human Papilloma Virus (HPV), Tdap, MMR-V, MCV4
- Increased focus on adolescents and adults
  - Meningococcal, varicella, HPV vaccines
  - Different diseases/potential adverse events (autoimmune, stroke/M.I.)
- Study of rare adverse events require even larger infrastructure
  - Guillain-Barré syndrome
- Public perception regarding safety of vaccines
- Future vaccines
  - Herpes, Cancer, Chronic diseases

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Ensuring the Safety of Vaccines in the 21st Century

Structure
- Create strategic plan for ISO
- Establish broad input into the research agenda for ISO
  - External advisory panel based in NVPO

Science
- Active surveillance of new vaccines
  - 'Real-time' assessments of vaccine safety
- Pandemic influenza preparedness
  - Need to substantially increase safety infrastructure
- Personalized medicine and vaccine safety
  - ISO uniquely situated to study which persons/subgroups are at increased risk for VAE

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