**F. Edward Yazbak, MD, FAAP**
**70 Viewcrest Drive, Falmouth, MA 02540**
**Tel (508) 540 5060 - Fax (508) 457 9814**
**TLAutStudy@aol.com**

**"What we have in us of the image of God is the love of truth and justice."**
**-- *Demosthenes***

**Case: Alan Yurko**

**Evidentiary Hearing**

**August 2004**

# VAERS

# Uses and Limitations

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# How the CDC, FDA, Others Use VAERS

# The Vaccine Adverse Event Reporting System

**The CDC and FDA (Federal Drug Administration) warn about misinterpretation of VAERS reports and data**

**When evaluating data from VAERS, it is important to note that for any reported event, no cause and effect relationship has been established. VAERS is interested in all potential associations between vaccines and adverse events. Therefore, VAERS collects data on any adverse event following vaccination, be it coincidental or truly caused by a vaccine. The report of an adverse event to VAERS is not documentation that a vaccine caused the event.**

**The above statement is clear.**

**The fact that a doctor, a nurse, a patient or a drug manufacturer reports an adverse event to VAERS does NOT mean that the specific adverse event reported is absolutely and without doubt due to the vaccine that was administered.**

**The FDA and CDC have spent millions of dollars to design and implement VAERS because, as stated above, it is important to detect any association between vaccines and adverse events, whether causal or coincidental. Experts can look at trends, examine them thoroughly and assist the Agencies in formulating the appropriate recommendations. For example, when VAERS received the first report that a baby had an intussusception and died after receiving the Rotashield (Rotavirus) vaccine, there was no immediate reaction. When many reports arrived in a short time, the use of the vaccine was halted and a short while later, the vaccine was appropriately withdrawn from the market.**

**When thousands of reactions following DTP (Diphtheria, Tetanus and Pertussis) vaccination were reported to VAERS, the decision was made to switch to the DTaP, which contained an acellular pertussis component instead of the problematic whole cell vaccine that had been used for decades in the United States.**

**Similarly, after multiple reports of paralysis were reported to VAERS following oral polio vaccination, the OPV was withdrawn from the US market and the inactivated polio vaccine (IPV) was reintroduced.**

**The American Academy of Pediatrics (AAP) and the CDC frequently remind pediatricians of the importance of VAERS reporting and how crucial is the information derived from VAERS, in the monitoring of national vaccination programs.**

**I have carried out several reviews of VAERS reports in preparation for my testimony at the Alan Yurko Evidentiary Hearing. For the sake of brevity, I will only include the following references to clearly show the Court that the CDC, the FDA and outside investigators use VAERS data all the time.**

**<u>Reference I</u>**

**In my main presentation, I start the discussion of my VAERS research by quoting the objectives of the CDC as listed in the February 14, 2003 MMWR (Mortality and Morbidity Weekly Report).**
**[MMWR Morb Mortal Wkly Rep. 2003 Feb 14;52(06):113 by - Zhou W. et.al.]**

**Those objectives are to**

1) **Detect new, unusual, or rare vaccine adverse events**
2) **Monitor increases in known adverse events**
3) **Determine patient risk factors for particular types of adverse events**
4) **Identify vaccine lots with increased numbers or types of reported adverse events; and**
5) **Assess the safety of newly licensed vaccines.**

**The complete report is 49 pages long and includes a review of the 128,717 reports to VAERS between January 1, 1991 and January 1, 2002. Only a portion is included as Reference I.**
**The following quotes are relevant:**

***Interpretation: As a national public health surveillance system, VAERS is a key component in ensuring the safety of vaccines. VAERS data are used by CDC, FDA, and other organizations to monitor and study vaccine***

***safety. CDC and FDA use VAERS data to respond to public inquiries regarding vaccine safety, and both organizations have published and presented vaccine safety studies based on VAERS data. VAERS data are also used by the Advisory Committee on Immunization Practices and the Vaccine and Related Biological Products Advisory Committee to evaluate possible adverse events after vaccinations and to develop recommendations for precautions and contraindications to vaccinations. Reviews of VAERS reports and the studies based on VAERS reports during 1991--2001 have demonstrated that vaccines are usually safe and that serious adverse events occur but are rare."***

***"Public Health Actions: Through continued reporting of adverse events after vaccination to VAERS by health-care providers, public health professionals, and the public and monitoring of reported events by the VAERS working group, the public health system will continue to be able to detect rare but potentially serious consequences of vaccination. This knowledge facilitates improvement in the safety of vaccines and the vaccination process."***

***Introduction***

***The National Childhood Vaccine Injury Act (NCVIA) (1) of 1986 required health professionals and vaccine manufacturers to report to the U.S. Department of Health and Human Services specific adverse events that occur after the administration of routinely recommended vaccines. Postvaccination adverse events and the time frames in which they must occur to qualify as being reportable under NCVIA are listed in the Reportable Events Table (2). The table is updated periodically as the vaccination schedule changes, new vaccines are introduced, and new vaccine-associated adverse events are identified. Vaccine-associated adverse event reports were previously collected separately by CDC and the Food and Drug Administration (FDA). CDC maintained the Monitoring System for Adverse Events Following Immunization (3) for vaccines administered in the public sector; FDA maintained the Spontaneous Reporting System (4) to accept reports from both the public and private sectors, although it was used primarily by vaccine manufacturers. These systems were replaced by the Vaccine Adverse Event Reporting System (VAERS) on November 1, 1990 (5). Under the joint administration of CDC and FDA, VAERS accepts spontaneous reports of suspected vaccine***

***adverse events after administration of any vaccine licensed in the United States (6--9).***

***Unlike many surveillance systems that monitor a single exposure and its associated outcomes, VAERS monitors multiple exposures (i.e., different vaccines often administered simultaneously in different combinations) and an increasing number of potential outcomes. VAERS accepts spontaneous reports from health professionals, vaccine manufacturers, and the public. Reports are submitted by mail or fax. In 2002, electronic reporting to VAERS through the Internet became available by accessing http://secure.vaers.org/VaersDataEntryintro.htm. All reports, whether submitted directly to VAERS by an individual or by state or local public health authorities or manufacturers, are entered into the VAERS database.***

***Federal regulations require that each manufacturer with a product license from FDA report the following adverse events to VAERS: all spontaneous reports of adverse experiences occurring within the United States, whether serious, nonserious, expected or unexpected, and all serious and unexpected adverse experiences occurring outside of the United States or reported in scientific and medical journals as case reports or as the result of formal clinical trials (10). Data collected on the VAERS form (11) include information regarding the patient, the vaccine(s) administered, the reported adverse event, and the person reporting the event. Federal regulations (10) define serious events as those involving death, life-threatening illness, hospitalization or prolongation of hospitalization, or permanent disability. All reports with adverse events classified as serious are followed up with a request for additional information (e.g., medical records and autopsy reports) to provide a complete description of the case. For all original and follow-up reports, the signs, symptoms, and diagnoses mentioned in the description of the adverse event are coded using FDA's Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) (12). All information is stored in a computerized database for subsequent reference and analyses. All reporters receive written acknowledgment of receipt of their reports along with a request for missing information where indicated. In addition, letters to obtain information regarding the recovery status of persons with serious adverse events are mailed to the reporters at 60 days and 1 year after vaccination.***

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**Reference II**

**In a personal letter from the office of the Assistant Surgeon General and Director of the CDC's National Immunization Program in 1999, it is clearly mentioned that autism is rare and that an autism-vaccine connection did not exist because only 15 cases of autism after vaccination had been reported to VAERS in 8 years.**

**This shows that the CDC used VAERS data, found the derived information reliable and could formulate a scientific opinion based on those reports.**

**Obviously if 3,000 VAERS reports of autism following vaccination had been filed in 8 years, then the CDC could not have stated that a vaccine-autism connection did not exist.**

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**Reference III**

**"Neonatal Deaths after Hepatitis B Vaccine, The Vaccine Adverse Event Reporting System, 1991-1998.**
**(Arch Pediatr Adolesc Med. 1999;153:1279-1282).**
**Manette T. Niu, MD, Division of Biostatistics and Epidemiology, Center for Biologic Evaluation and Research, Food and Drug Administration.**

**The purpose of the study was to evaluate reports filed with VAERS, from January 1, 1991 through October 5, 1998, of neonatal deaths (0-28 days of age) after hepatitis B vaccination.**
**There were 1771 neonatal reports in all and 18 deaths. The authors estimated that around 86 million doses of the vaccine were administered and concluded that: *"while the limitations of passive surveillance systems do not permit definitive inference, these data suggest that HepB immunization is not causing a clear increase in neonatal deaths."***

**Again, if there had been 18,000 neonatal deaths during those seven years instead of 18, then the data in VAERS would have suggested that hepatitis B vaccination was indeed a clear factor in the increase.**

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**Reference IV**

**Descriptive epidemiology of adverse events after immunization: reports to the Vaccine Adverse Event Reporting System (VAERS), 1991-1994.**
**Braun MM, Ellenberg SS. Division of Biostatistics and Epidemiology, FDA.**
**J Pediatr. 1997 Oct;131(4):529-35.**

**A total of 38,787 adverse events were reported VAERS 1991-1995**
***"The large number of reports and national coverage of the Vaccine Adverse Events Reporting System make it useful for monitoring the safety of vaccine lots and for accumulating case series to detect or better understand adverse events that may occur too rarely to be assessed in clinical trials or in the larger studies that are sometimes carried out by manufacturers after vaccine licensure."***

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**Reference V**

**Pediatric deaths reported after vaccination: the utility of information obtained from parents.**
**Silvers LE, Varricchio FE, Ellenberg SS, Krueger CL et.al. (FDA)**
**Am J Prev Med. 2002 Apr;22(3):170-6.**

**The study was designed to follow up 100 consecutive pediatric deaths reported to VAERS by interviewing a parent and a healthcare provider (HCP) for each case.**

**One of the conclusions was: *"In some instances, parents were more likely than HCPs* (Health Care Providers) *to provide information regarding some important variables about the nature of the death."***

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**Reference VI**

**Comparative safety of two recombinant hepatitis B vaccines in children: data from the Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink (VSD).**
**Niu MT et.al**
**Center for Biologic Evaluation and Research, FDA**
**J Clin Epidemiol. 1998 Jun;51(6):503-10.**

**In this study, the FDA wanted to compare two brands of hepatitis B vaccine. The authors relied in their research on passive reports to VAERS and to the Vaccine Safety Datalink (VSD).**

**The conclusion re 1991 to 1994 VAERS reports is clear.**
***"Our investigation reveals that it is unlikely there is a true difference between rates of serious events temporally associated with the two HepB vaccines in children. This study demonstrates the dual roles played by VAERS and VSD in providing a more complete picture of the post-marketing safety profile of childhood vaccines, and underscores the importance of using other analytic studies to evaluate findings from passive surveillance systems of adverse events."***

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**Reference VII**

**Infant immunization with acellular pertussis vaccines in the United States: assessment of the first two years' data from the Vaccine Adverse Event Reporting System (VAERS).**
**Braun MM, Mootrey GT, Salive ME, Chen RT, Ellenberg SS. (FDA) Pediatrics. 2000 Oct;106(4):E51.**

***"A comparison of the adverse event profiles (proportional distributions) for DTaP, DTP, and DTPH, as well as an analysis of specific adverse events considered in a 1991 Institute of Medicine report on the safety of diphtheria-tetanus-pertussis vaccine, did not identify any new, clear safety concerns. CONCLUSIONS: These findings reflect the administration of millions of doses of acellular pertussis vaccine and are reassuring with regard to the safety of marketed acellular pertussis vaccines. VAERS data, although subject to the limitations of passive surveillance, support the prelicensure data with regard to the safety of the US-licensed acellular pertussis vaccines that we evaluated."***

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**Reference VIII**

**Clinical implications of endotoxin concentrations in vaccines.**
**Geier DA, Geier MR. Genetic Centers of America, Silver Spring, MD**
**Ann Pharmacother. 2002 May;36(5):776-80**
***"The vaccines analyzed with the LAL assay were whole-cell DTP vaccine lots manufactured by Connaught, Lederle, the Michigan and Massachusetts Departments of Health, and Wyeth; DTaP vaccine lots manufactured by Merieux and Takeda; and DT vaccine lots manufactured by Wyeth and Lederle. The incidence of adverse reactions following whole-cell DTP, DTaP, and DT vaccines were determined based on analysis of the Vaccine Adverse Events Reporting System (VAERS) database."***

**Endotoxin levels of three vaccines were tested independently and compared to VAERS reports related to those specific vaccines. The authors were then confident to conclude that DTP was more virulent and caused more reactions than DTaP and DT.**

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**Reference IX**

**Gastrointestinal reactions and rotavirus vaccination based upon analysis of the Vaccine Adverse Events Reporting System (VAERS) database for 1999. A model for the calculation of the incidence rates and statistical significance of adverse events following immunization.**
**Geier DA, Geier MR. MedCon, Inc., USA.**
**Hepatogastroenterology. 2004 Mar-Apr;51(56):465-9**
***"CONCLUSIONS: This analysis demonstrated that the VAERS database provides a way to detect whether RRV-TV elevates the risk of adverse reactions compared to control vaccines given to similar age groups when appropriate denominators (number of annual doses given) are employed. Because of its massive size and the availability of numerous vaccine control groups, the VAERS database provides data on adverse reactions following vaccination that is available nowhere else"***

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**Reference X**

**Data mining in the US Vaccine Adverse Event Reporting System (VAERS): early detection of intussusception and other events after rotavirus vaccination.**

**Niu MT, Erwin DE, Braun MM. Vaccine Safety Branch, FDA. Vaccine. 2001 Sep 14;19(32):4627-34.**

***"Empirical Bayesian data mining, a data analysis method, utilizes the number of events reported for each vaccine and statistically screens the database for higher than expected vaccine-event combinations signaling a potential vaccine-associated event. This is the first study of data mining in VAERS designed to test the utility of this method to detect retrospectively a known side effect of vaccination-intussusception following rotavirus (RV) vaccine. From October 1998 to December 1999, 112 cases of intussusception were reported. The data mining method was able to detect a signal for RV-intussusception in February 1999 when only four cases were reported. These results demonstrate the utility of data mining to detect significant vaccine-associated events at early date. Data mining appears to be an efficient and effective computer-based program that may enhance early detection of adverse events in passive surveillance systems."***

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**On June 26, 2004 I accessed the CDC website www.cdc.gov and searched for VAERS. There were 566 documents. The six pages entered as Reference XI represent the first page and contain over 60 studies and reports. The most recent entry is dated June 14, 2004 and is actually Reference I of this presentation.**

**The third entry of the first page of the CDC VAERS search was posted on June 11, 2004. It is introduced as Exhibit XII.**

**Vaccine Safety Post-Marketing Surveillance: The Vaccine Adverse Event Reporting System (VAERS): *"The National Immunization Program is sponsoring a continuing education activity (#SS3092) entitled Vaccine Post-marketing Surveillance: The Vaccine Adverse Event Reporting System"… In order to receive these credits, you must complete this educational activity using the CDC Training and Continuing Education Online system by September 19, 2004."***

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*In conclusion*

**The CDC and the FDA have a huge investment in the VAERS program; Both agencies have used, still use and will use VAERS data and have encouraged parallel research using information from the reports.**

**The National Immunization Program and the National Vaccine Advisory Board have relied on VAERS reports when formulating vaccine practices.**

**The National Vaccine Compensation Program has awarded indemnification based on evidence obtained from VAERS data. I was personally an expert witness in such a case.**

**I have written four research papers based on VAERS analyses.**

**Relative to my testimony at the Alan Yurko Evidentiary Hearing, I would like to assure the Court that I am fully aware of the rules of interpretation of VAERS data. I will carefully limit my testimony to a review of the vaccines that Baby Alan Yurko received, a review of similar cases reported to VAERS and information concerning some cases reported to the program as "Shaken Baby Syndrome".**

**Respectfully submitted,**

**_____ Date _____**

**F. Edward Yazbak, MD, FAAP**