A MEDWATCH CONTINUING EDUCATION ARTICLE

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# Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS)

## Learning Objectives:

Upon completion of this program, health professionals should be able to:

- Identify the principles of post-marketing surveillance
- Understand the objectives of VAERS
- Understand how VAERS operates
- Discuss basic limitations and strengths of data derived from VAERS
- List examples of FDA regulatory actions that have been based on post-marketing passive surveillance
- Describe how FDA disseminates information regarding vaccine safety to the public
- Understand how clinical practice impacts a national post-marketing surveillance system

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## BENEFITS AND RISKS OF IMMUNIZATION

Over ten million childhood vaccinations are given to children (birth through 5 years) annually, and many million of doses are given to adults. All medicinal products, including vaccines, have risks and benefits. Vaccines protect many people from dangerous illnesses, but, like drugs, can cause side effects, a small percentage of which may be serious. The benefit of vaccines is measured as prevented disease, and the risk of vaccination is measured as potential side effects; both are monitored as part of the US public health system.

## PRE-LICENSURE EVALUATION OF VACCINES

Licensure requires extensive clinical evaluation of the vaccines' safety and effectiveness which is completed in stages over several years. First, laboratory and animal studies are performed. Then candidate vaccines are tested in small groups of adult volunteers to establish first the safety, and then, the efficacy of the vaccine. Finally larger-scale clinical trials, usually randomized and placebo-controlled, measure the rates of the more common adverse events and the protective efficacy of the vaccine. The control groups in these clinical trials who do not receive vaccine are critical to distinguishing between vaccine-related events and an event unrelated to vaccine but occurring spontaneously in the study population. Rates of the most common vaccine reactions, such as injection site reactions and fever, can be estimated before licensure, but the comparatively small number of patients enrolled in these trials generally limits detection of rare events or events that occur after long-term exposure. Even the largest pre-licensure trials (>10,000 persons) are inadequate to assess the vaccine's potential to induce rare but serious side effects. Consequently, it is essential to continue to collect information on vaccine-associated adverse events after licensure which may only occur after wide-scale use of the vaccine in the general population.

## POST-MARKETING SURVEILLANCE

Post-marketing surveillance is a necessary component of vaccine safety monitoring. The manufacturers' label/product information approved at licensure has the potential to be continuously updated as significant adverse event information which differs from what was originally known at the time of approval is compiled. Due to the relatively small number of patients studied in pre-licensure studies, rarer side effects or events that may only occur in a sub-group of the population not significantly represented in pre-marketing studies (e.g., neonates and infants who receive hepatitis B vaccine, pregnant women, immunosuppressed patients), or side effects that occur only with chronic or repeated exposure to a vaccine-induced antigen may not be revealed until the vaccine is licensed to the general public.

Pre-licensing clinical trials are conducted in a controlled environment, much different from data obtained from passive or active post-marketing surveillance systems. After licensure, vaccinated persons have diverse demographic characteristics (e.g., age, race, socioeconomic background), medical history (immunocompromised host), and/or multiple medical problems necessitating medication (potential drug interactions). These previously unstudied components of a patient's social or medical history may be risk factors which could impact the outcome of vaccination and contribute to the development of adverse events. Thus, when the product leaves the controlled study environment of

clinical trials and is put into general clinical use by practitioners, the ability to determine the actual incidence of adverse events is questionable.

The objectives of post-marketing surveillance are to identify rare adverse reactions not detected during pre-licensure studies, monitor increases in known reactions, identify risk factors or pre-existing conditions that may promote reactions, and identify particular vaccine lots with unusually high rates or types of events.

There are two types of post-marketing surveillance systems typically in use: active and passive surveillance. Active surveillance links the vaccination status of all persons in a defined population to their clinical outcomes, thus, minimizing under-reporting. Such a system may provide comprehensive data, but may be very expensive and due to the comparatively small number of participants, may lack ability to detect very rare events or deaths. Passive surveillance systems rely on health professionals or vaccinees to voluntarily submit reports of illness following vaccination. There is no solicitation of these reports; this system is simpler, less expensive, does not limit the population from which reports are accepted, and because of the broad pool of reporters, offers the potential for detecting rare events. However, limitations of passive surveillance systems include variability in reporting standards, reporter bias and significant under-reporting of events. Both active and passive surveillance systems lack specificity, that is, reported post-vaccination events may be coincidental and not caused by the vaccine.

Associating causality of reported post-vaccination events with a specific vaccine is challenging and requires careful weighing of all the scientific evidence, evaluation of the quality and consistency of the data, and consideration of biologic plausibility of the association between vaccination and event (Table 1)(1,2,17). The stronger the vaccine-event relationship in each case, and rarer the spontaneous incidence of the event (i.e., background rate in an unvaccinated population), the fewer cases are needed to establish a causal association (1,2,17). Biologic plausibility and strength of association aid in evaluating if an association is causal, as does a vaccination re-challenge ("positive rechallenge") which elicits an identical vaccine reaction (1,2).

When faced with a suspicious event, it is important to try to determine the background incidence rate of the event before making a judgement as to causality (1,2). Defining the relationship between vaccine exposure and the occurrence of an event is not easy, and it is often impossible with the available data to reach a conclusion. Since events may act through the same physiological and pathological pathways as normal disease, they are difficult to distinguish. The causal association between vaccination and event may be suggested by various criteria (Table 1)(1,2,17).

## VACCINE SAFETY SURVEILLANCE: VAERS

The National Childhood Vaccine Injury Act (NCVIA) of 1989 requires health professionals and vaccine manufacturers to report to the Department of Health and Human Services (DHHS) specific adverse events following the administration of vaccines specified in the Act. The Reportable Events Table, part of the Act, lists reportable post-vaccination events and the time frames in which they must occur in order to qualify as being reportable (Table 2)(17). In 1990, DHHS established the Vaccine Adverse Event Reporting System (VAERS), co-administered by the Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) to accept all reports of suspected adverse events after administration of any U.S. licensed vaccine.

VAERS, the national passive surveillance system monitoring vaccine safety, is a system to which clinical events after vaccination are voluntarily reported from health professionals, vaccine manufacturers, and the public (2,3). The reports are submitted to state or local public health authorities, vaccine manufacturers, or directly to VAERS, and all ultimately end up in the VAERS database. Food and Drug Regulations (21 CFR section 600.80) currently require that the following adverse events be reported to VAERS by each manufacturer having a product license from FDA: all spontaneous reports of adverse experiences occurring within the U.S., whether serious, non-serious, expected or unexpected; and all serious and unexpected adverse experiences occurring outside of the U.S. or reported in scientific/medical journals as case reports or as the result of formal clinical trials (Table 2)(17).

In order to encourage reporting of adverse events, FDA regulations offer substantial protection against disclosure of the identities of both reports and patients. Since July 3, 1995, a regulation preempted state discovery laws regarding voluntary

TABLE 1

### EVALUATING SIDE EFFECTS AFTER VACCINATION: TEMPORAL VERSUS CAUSAL ASSOCIATIONS (17)

*An adverse event can be causally attributed to vaccine more readily if:*

1. Chronology of administration of agent, including beginning and ending of treatment and adverse event onset is known
2. Previously known toxicity of agent
3. Event conforms to a specific clinical syndrome whose association with vaccination has strong biologic plausibility (e.g., anaphylaxis)
4. Laboratory result confirms association (e.g., isolation of vaccine strain varicella vaccine from skin lesions of a patient with rash)
5. Event recurs on re-administration of vaccine ("positive rechallenge.")
6. Controlled clinical trial or epidemiologic study shows greater risk of adverse events among vaccinated vs unvaccinated (control) groups

reports held by pharmaceutical manufacturers.

## LIMITATIONS AND STRENGTHS OF VAERS

VAERS is subject to limitations inherent to passive surveillance systems (2,3). Nevertheless, the national VAERS has been successful in identifying vaccine-associated events that serve as hypotheses to be tested or further investigated in more rigorously controlled studies, such as the CDC's Vaccine Safety Datalink (VSD) (a computerized medical record linkage system of patients enrolled in 4 health maintenance organizations [HMOs]), where causality may be better determined (2-11).

### Limitations of VAERS

#### *Under-reporting*

VAERS receives only a portion of the total number of events ("numerator") which occur after vaccination (2,3,7,9,13). Computing reporting rates from VAERS may be misleading, since the extent of under-reporting is unknown. Compounding the problem of under-reporting is the lack of precise data as to the number of vaccine doses administered in the population ("denominator") or the number of persons at risk for the adverse event of interest. These limitations make incidence rates computed from spontaneously reported data problematic (2,3,7,9). In addition, VAERS does not receive reports for background events in unvaccinated persons--there is no control group with whom to compare event rates in the vaccinated vs. unvaccinated population (2,3,9).

Given the limitations of VAERS (e.g., lack of accurate information as to the number of vaccine doses administered in the population, lack of control group, reporting bias, incomplete data, lack of consistent diagnostic criteria for disease, and indirect influences accorded sale of vaccine to government contracts in public sector and the manufacturers market share of vaccine), VAERS is a crude tool which may at best estimate reporting rates of events based on manufacturer distribution date (propriety information available only to FDA and vaccine manufacturer), that serves as a signal suggesting hypotheses to test in methodologically more rigorous databases (2-11).

#### *Deficient data quality*

The ability to assess, analyze and act on safety issues based on spontaneous reporting is dependent on the quality of information submitted by reporters. Clinical details and diagnosis of a given report may be inaccurate, non-specific or missing. The quality of the data depends upon the reporter, who may lack clinical training, or who may not have access to complete clinical information. Since VAERS receives an estimated 12,000 reports annually, it is difficult to ensure the accuracy and completeness of the database with available resources, although checks are performed for a few key data items (e.g., type of vaccine, event severity).

TABLE 2

**ADVERSE EVENT (AE) REPORTING REQUIREMENTS FOR VACCINE MANUFACTURERS (17)**

1. 15-day Alert reports: serious and unexpected (i.e., not in the product's current labeling) must be reported to FDA within 15 working days.
2. Periodic AE reports: all non-15 day AE reports must be reported periodically (quarterly for the first three years after approval, then annually).
3. Scientific literature: a 15-day report based on scientific literature (case report; results from a formal clinical trial; epidemiology-based studies or "analyses of experience in a monitored series of patients").
4. Post-marketing studies: pharmaceutical causation for AE "reasonable possibility."

#### *Simultaneous administration of multiple vaccine antigens*

Following the current recommendations for childhood vaccines, reports often involve administration of multiple vaccine antigens, making identification of the role of a specific vaccine in an adverse event difficult (2,3,7,9).

#### *Reporting bias*

Spontaneously reported information is uncontrolled and subject to the possible influence of a number of biases that can affect reporting. Biases include length of time a product has been on the market (e.g., increased reporting rates the first 2 years a new vaccine is licensed), temporal reporting biases (e.g., events that occur within 4 weeks of vaccination are more likely to be reported) and reporting environment (e.g., increased reporting with news coverage and from the public vs private sector), individual biases (e.g., vaccinee convinced vaccine responsible for adverse event--initiating VAERS report or lawsuit)(2).

#### *Inclusion of events not causally related to vaccination*

All reports are entered into the VAERS database regardless of confirmed or possible alternative explanations as to the cause of illness. Temporal association by itself does not mean that the vaccine caused a symptom or event as the event may be purely coincidental (1-3). Because of the large number of vaccine exposures, events temporally associated with vaccine will occur. With multiple childhood vaccines (diphtheria-tetanus-acellular pertussis [DTaP], oral polio virus [OPV]/inactivated polio virus [IPV], hemophilus influenzae type B virus [HIB]), administered to nearly all infants starting at two months of age, most health problems in infancy, whatever their cause, will occur in vaccinated children, some of which will by chance occur in recently vaccinated children (2).

An adverse event may be causally attributed to vaccination more readily if certain conditions are met (Table 1). Because few adverse events reported to VAERS meet these criteria, epidemiologic evidence is the basis for assessing causality for the most serious adverse events investigated. Determination if the vaccine caused the

post-vaccination event usually cannot be made on the basis of information acquired from individual VAERS reports, and needs confirmation in other methodologically more rigorous databases (e.g., VSD), or clinical trials (2,3,11).

### Strengths of VAERS

Although VAERS has methodologic limitations inherent in passive surveillance systems such as under-, biased-, and incomplete reporting, lack of consistent diagnostic criteria, lack of a comparison (control) group, and lack of data as to the precise number of doses of vaccine administered to the population, VAERS has strengths essential to the U.S. vaccine safety monitoring system (2,3). It is the only surveillance system which covers the entire U.S. population,includes the largest number of case reports of events temporally associated with vaccination in the U.S., and can assess the safety of specific vaccine lots. Other strengths include the timely availability of data from a geographically diverse population, the ability to detect possible new, unusual or rare adverse events and to generate hypotheses that may be tested in other databases (2,3). Spontaneous report-based surveillance programs perform an important function by generating signals of potential problems that may warrant further investigation.

VAERS is the "front line" of national vaccine safety surveillance and is especially valuable in assessing the safety of newly marketed vaccines and rare events (2,3). Careful review of reports during the initial months of licensed use can provide additional assurance about the safety of a new vaccine, uncover previously unexpected events which occur when a vaccine is used in a new sub-group, or rapidly identify problems not observed during prelicensure. Recent reviews re-affirm the safety of hepatitis B vaccines in neonates and infants (7), and hepatitis A vaccine in the general population (8).

## OVERVIEW OF VAERS

VAERS receives approximately 12,000 reports annually, and since 1991 has received at least 75,000 reports. However, VAERS solicits reports of events not only known to be causally related to vaccine but all events temporally related to immunization, a portion of which may be coincidental. Data collected on the VAERS form include age, sex, birth weight (in patients younger than 6 years), date of vaccination, type of vaccine, manufacturer, lot number, number of previous doses of vaccine, date of onset of symptoms, and clinical description of the event (Figure 1). Events are classified by severity: death, serious (Table 3), and non-serious. About 15% of reports describe serious events, and 85% are non-serious. An "unexpected" event is an event not noted in the FDA-approved manufacturers'labeling of the vaccine. All reports of deaths and serious events received by the FDA are followed-up by telephone and/or written inquiry by FDA staff or VAERS contractor. Letters to follow-up serious reports and obtain the recovery status are mailed to the reporters at 60 days and 1 year after vaccination. The signs, symptoms, and diagnoses mentioned in the narrative description of the adverse event is coded using FDA's Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART). All information obtained from the original and follow-up VAERS report is entered as computerized data and stored in a relational database for subsequent analysis.

The VAERS database, excluding patient identifiers, is available to the public from the National Technical Information Service (NTIS), telephone: (703) 487-4650, or Freedom of Information (FOI) staff can respond to requests for portions of the database or redacted copies of VAERS forms, telephone: (301) 827-2000. General information and the VAERS form itself are available on the VAERS Internet website:
http://www.fda.gov/cber/vaers.html.

Based on careful review of spontaneous reports, FDA can initiate various actions: manufacturers' labeling or packaging change(s), conducting or requesting manufacturer-sponsored post-marketing epidemiologic investigations (hypotheses testing in more rigorous databases) (2,3,11), issuing a Safety Alert or "Dear Health Professional" letter, inspecting manufacturers' facilities/records, or working with a manufacturer regarding possible withdrawal of vaccine from the market (for safety or efficacy reasons). Keeping vaccine labeling/package inserts up-to-date is an ongoing, dynamic process that depends on new information gleaned from spontaneous adverse event reports.

Dissemination of safety-related information to health care professionals and the public is an important public health goal of post-marketing surveillance.

## OBJECTIVES OF VAERS AND RESULTS OF ANALYSES OF VAERS DATA

### *Identification of new, rare vaccine reactions, increased rates of known side effects, risk factors for adverse events*

Several investigations based on VAERS data have uncovered previously unrecognized problems that may occur in vaccine recipients, including: rare life-threatening thrombocytopenia after measles-mumps-rubella (MMR) vaccination (Box 1) (4), hair loss after hepatitus B vaccination (Box 2) (5), serious injuries resulting from vaccine-induced syncope or fainting (Box 3) (6), and identification of the low risk of convulsions following receipt of DTP and measles-containing vaccines (10). VAERS can also be used to evaluate the safety of vaccinating a new sub-group of the population (e.g., universal immunization of infants with hepatitis B vaccine

TABLE 3

**FDA CLASSIFICATION OF SERIOUS VAERS EVENT:**

*An event with one of the following patient outcomes:*

1. Fatal
2. Life-threatening
3. Persistent or significant disability/incapacity
4. Requires or prolongs hospitalization
5. Congenital anomaly/birth defect
6. Requires intervention to prevent an outcome listed above

after the vaccine had been initially used in adult health care workers)(7), assessing the safety of newly licensed vaccines (e.g., hepatitis A [8] , varicella [FDA, unpublished data], DTaP [10]), or comparing the safety of two brands of vaccine (9).

### *Identification of vaccine lots with increased numbers of types of reported events*

Since 1993, FDA staff have performed weekly review of the numbers and types of reported events in specific vaccine lots based on distribution data provided by vaccine manufacturers (proprietary data). Evaluating lot-specific reports is problematic as vaccine lot size greatly varies (range: 3,000-700,000 doses), and more reports are usually received for a large lot than a small one. To date, no lot has been found to be unsafe. This result is not surprising given the stringency of the manufacturing and testing requirements to which vaccines are subject. Nevertheless, because of the possibility of such a problem arising, regular attention to lot-specific reports is an important aspect of FDA's program of vaccine safety monitoring.

There have only been four FDA-initiated recall of vaccines since 1987: One lot was recalled after FDA detected particulates, another lot was mislabeled, the third was recalled because of violations in manufacturing practices at a production plant that was found after an FDA inspection, and the fourth was because of a decrease in vaccine potency over time.

## POST-MARKETING REPORTING OF ADVERSE EVENTS: THE CRITICAL ROLE OF HEALTH PROFESSIONALS

The FDA has the regulatory responsibility to ensure the safety of vaccines. Determination of whether an event was caused by the vaccine is not a pre-requisite for filing a VAERS report. VAERS solicits reports for all events temporally related to vaccination, some of which may be coincidental (1-3). Any index of suspicion that a serious event or death may be related to vaccination is reason for the health professional to submit a VAERS report. The role of the health professional in supporting the national passive surveillance system is essential, as the first hint of a potential problem usually originates with the astute clinician who reported the case to the appropriate source. Post-marketing surveillance relies on health professionals to report suspicious events, thus improving the quality of reported data, and contributing significantly to safeguarding public health in vaccine safety.

BOX 1:

### SEVERE THROMBOCYTOPENIA AFTER MMR II IMMUNIZATION (4)

A cluster of VAERS reports of severe thrombocytopenia (TP) after MMR II immunization prompted FDA review. 55 reports coded thrombocytopenia or thrombocytopenia purpura were retrieved from 8,581 reports for measles-containing vaccines. 55% occurred in children < 2 years old (range 1-40 years) and cases were evenly distributed between males and females. 42 reports noted onset of symptoms 3 to 32 days after vaccination (median time to diagnosis, 12 days), 41 cases necessitated hospitalization, 17 patients were treated with intravenous immunoglobulin and/or steroids and one 12 year-old male had splenectomy.

Two serious complications were reported: a 1 year-old male (platelet count, 1,000/$mm^3$, 12 days after immunization) had severe gastrointestinal hemorrhage requiring blood transfusions; a 15 month-old male (platelet count, 5,000/$mm^3$,) had pulmonary hemorrhage. There were 2 deaths: a 17 year-old male with history of recurrent TP secondary to antiphospholipid syndrome died from sepsis 4 days after immunization; a 4 year-old male died 7 days after receiving vaccine from Escherichia coli 0157:H7 infection complicated by pseudomembranous colitis.

Platelet counts reported for 42 persons ranged from 1,000 to 102,000 $mm^3$; 29 had platelet counts ≤20,000/$mm^3$. These findings suggest that individuals with a history of TP, regardless of etiology, may have recurrent episodes of TP after immunization, and deserve a careful risk-benefit analysis before receiving vaccine. These reports represent 0.07% of reports for measles-containing vaccines received by VAERS, and suggest that post-vaccination TP is a rare event.

BOX 2:

### HAIR LOSS AFTER IMMUNIZATION (5)

One day after a 30 year-old female nurse's first dose of hepatitis B (HepB) vaccine, she developed mild hair loss, arthralgias, fatigue and weakness which lasted 1 week. One day after her second HepB dose she had recurrent hair loss, and 2 weeks later, recurrent arthralgias, fatigue and weakness. Alopecia progressed for a few months until approximately half of her hair had a diffuse, thinned appearance. Her hair later regrew without treatment or workup.

BOX 3:

### SYNCOPE AFTER IMMUNIZATION (6)

697 cases of syncope after vaccination were reported. 77.4% were younger than 20 years, and 57.5% were female. Hospitalization was reported in 9.6%. Of the 571 syncope events with known interval to onset, 511 occurred 1 hour or less after vaccination, and 323 (63.2%) occurred within the first 5 minutes after vaccination. Tonic or clonic movements were reported in 30.4% of syncopal episodes occurring 15 minutes less, and in 12.8% of those occurring 15 minutes or longer after vaccination ($p<0.01$).

Six patients suffered skull fracture, cerebral bleeding or cerebral contusion after falls; 3 of these patients required neurosurgery. Falls occurred 15 minutes or less after vaccination in or near the clinic or office. Ages ranged from 12 to 28 years; 5 of 6 were male. Follow-up revealed substantial residual impairment in 2 patients.

Prevention of injury from syncope after vaccination may be possible. Vaccinators should be aware that patients exhibiting pre-syncopal signs and symptoms (hypotension, bradycardia, anxiety, pallor, cool clammy skin) around the time of immunization may need to be seated or lie down after immunization until free of symptoms.

## FDA EVALUATION OF REPORTS OF ADVERSE EVENTS

The uncontrolled nature of spontaneously reported data places great importance on the evaluation of submitted reports of adverse events. These analyses, applied on a case-by-case basis, are based on experience and knowledge of the vaccine being monitored and awareness of the limitations of the data. A major objective of the national VAERS is to disseminate vaccine safety information based on these analyses to the scientific community and the public through publications and presentation (2-16).

## COMPARISON OF VAERS AND MEDWATCH SURVEILLANCE SYSTEMS

FDA maintains two national passive surveillance systems monitoring the postmarketing safety of medicinal products: VAERS and MEDWATCH (a system which monitors the safety of medical products and devices that are not vaccines). Both systems mandate that manufacturers, distributors, pharmaceutical packers, and device user facilities of FDA-approved medical products report adverse events according to specific reporting requirements (Table 2).

## SUMMARY

The effectiveness of a national postmarketing surveillance program is directly dependent on the active participation of health professionals. Despite the limitations of spontaneous reports, FDA's program for vaccine surveillance provides vital information of clinical importance. The identification of signals in adverse event surveillance may initiate further investigation of potential problems in vaccine safety or efficacy, and the subsequent dissemination of safety-related information to the scientific community and the public. This process begins with and is dependent upon voluntary submission of reports of possible vaccine-associated events to VAERS by the astute, conscientious health professional.

TABLE 4

### HOW TO OBTAIN VAERS FORMS AND INSTRUCTIONS

**Copies of VAERS form (Figure 1) can be obtained from:**

VAERS
P.O. Box 1100
Rockville, Maryland 29849-1100

**Copies of VAERS form and instructions may also be obtained by:**

- Mail: Call 800-822-7967 or FAX request to: 877-721-0366
- If no access to 800 number: Call (301) 562-1086
- Internet: Visit the VAERS Website at www.vaers.org

**Where to send VAERS forms:**

VAERS
P.O. Box 1100
Rockville, Maryland 29849-1100

**Questions about reporting?**

Epidemiology Branch, ATTN: VAERS
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration
1401 Rockville Pike, HFM-210
Rockville, Maryland 20852-1448
Phone: (301) 827-3974
FAX: (301) 827-3529

# VAERS

## Vaccine Adverse Event Reporting System

***A Cooperative Program of the Centers for Disease Control and Prevention and the Food and Drug Administration***

**Call 1-800-822-7967 for VAERS Reporting Information**

VAERS

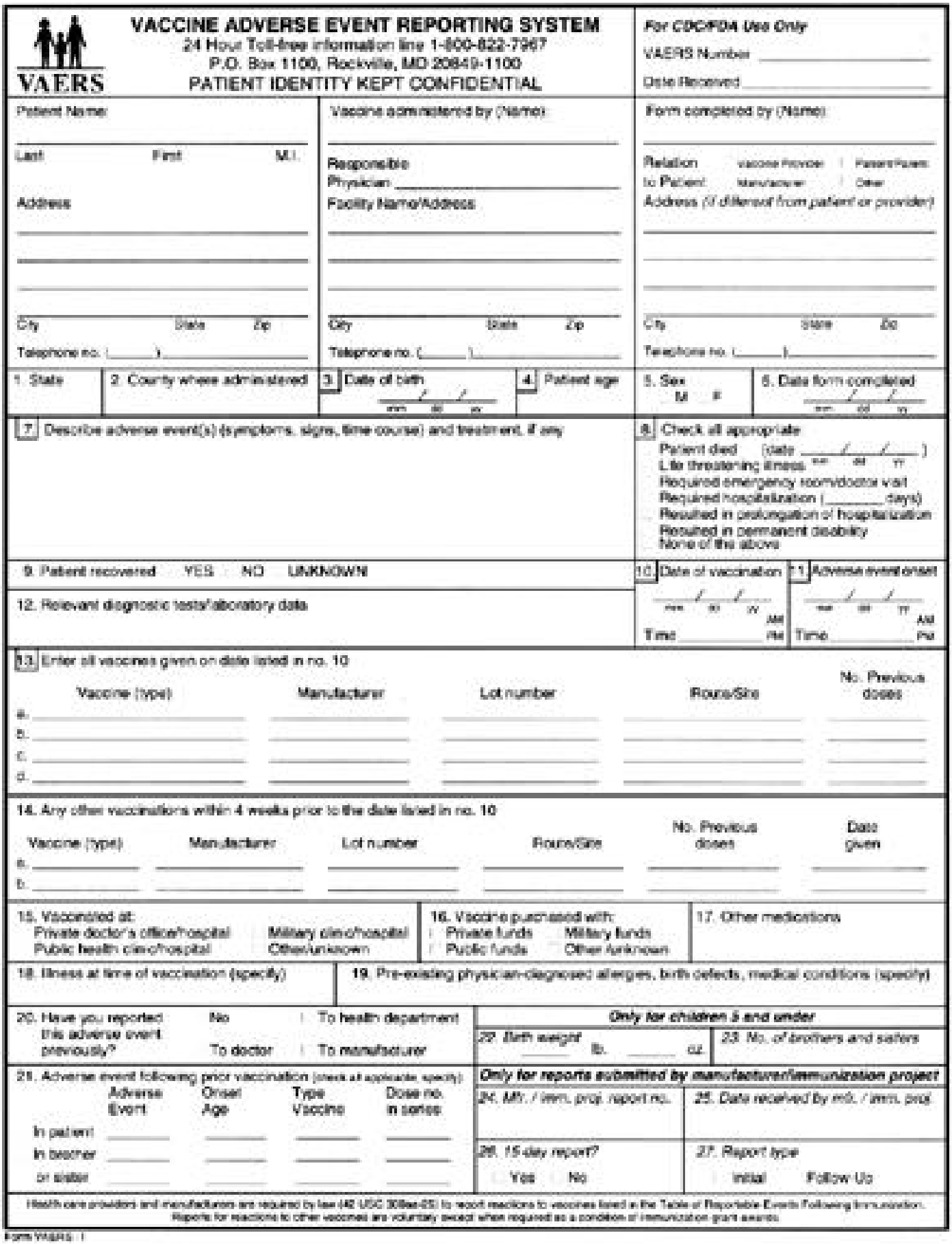
**VAERS**
**P.O. Box 1100**
**Rockville, MD 20849-1100**
**FAX: (877) 721-0366**

**VAERS E-mail: info@vaers.org Web: www.vaers.org**

**CDC NIP Website**
**http://www.cdc.gov/nip**

**FDA CBER Website**
**http://www.fda.gov/cber**

*Figure 1: VAERS Form*



**VACCINE ADVERSE EVENT REPORTING SYSTEM**
24 Hour Toll-free information line 1-800-822-7967
P.O. Box 1100, Rockville, MD 20849-1100
PATIENT IDENTITY KEPT CONFIDENTIAL

VAERS

For CDC/FDA Use Only
VAERS Number
Date Received

Patient Name: Last First M.I.
Address
City State Zip
Telephone no. ( )

Vaccine administered by (Name)
Responsible Physician
Facility Name/Address
City State Zip
Telephone no. ( )

Form completed by (Name)
Relation to Patient: Vaccine Provider / Parent/Parent / Manufacturer / Other
Address (if different from patient or provider)
City State Zip
Telephone no. ( )

1. State | 2. County where administered | 3. Date of birth (mm dd yy) | 4. Patient age | 5. Sex M F | 6. Date form completed (mm dd yy)

7. Describe adverse event(s) (symptoms, signs, time course) and treatment, if any

8. Check all appropriate
Patient died (date )
Life threatening illness
Required emergency room/doctor visit
Required hospitalization ( days)
Resulted in prolongation of hospitalization
Resulted in permanent disability
None of the above

9. Patient recovered YES NO UNKNOWN

10. Date of vaccination (mm dd yy) AM PM Time

11. Adverse event onset (mm dd yy) AM PM Time

12. Relevant diagnostic tests/laboratory data

13. Enter all vaccines given on date listed in no. 10

| | Vaccine (type) | Manufacturer | Lot number | Route/Site | No. Previous doses |
|---|---|---|---|---|---|
| a. | | | | | |
| b. | | | | | |
| c. | | | | | |
| d. | | | | | |

14. Any other vaccinations within 4 weeks prior to the date listed in no. 10

| | Vaccine (type) | Manufacturer | Lot number | Route/Site | No. Previous doses | Date given |
|---|---|---|---|---|---|---|
| a. | | | | | | |
| b. | | | | | | |

15. Vaccinated at:
Private doctor's office/hospital / Military clinic/hospital
Public health clinic/hospital / Other/unknown

16. Vaccine purchased with:
Private funds / Military funds
Public funds / Other/unknown

17. Other medications

18. Illness at time of vaccination (specify)

19. Pre-existing physician-diagnosed allergies, birth defects, medical conditions (specify)

20. Have you reported this adverse event previously? No / To health department / To doctor / To manufacturer

*Only for children 5 and under*
22. Birth weight lb. oz.
23. No. of brothers and sisters

21. Adverse event following prior vaccination (check all applicable, specify)

| | Adverse Event | Onset Age | Type Vaccine | Dose no. in series |
|---|---|---|---|---|
| In patient | | | | |
| In brother or sister | | | | |

*Only for reports submitted by manufacturer/immunization project*
24. Mfr. / imm. proj. report no.
25. Date received by mfr. / imm. proj.
26. 15-day report? Yes No
27. Report type Initial Follow Up

Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Table of Reportable Events Following Immunization. Reports for reactions to other vaccines are voluntary except when required as a condition of immunization grant awards.

Form VAERS 1

"Fold in thirds, tape & mail - DO NOT STAPLE FORM"

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES OR APO/FPO

**BUSINESS REPLY MAIL**

FIRST-CLASS MAIL PERMIT NO. 1995 ROCKVILLE, MD

POSTAGE WILL BE PAID BY ADDRESSEE

**VAERS**
P.O. Box 1100
Rockville MD 20849-1100

## DIRECTIONS FOR COMPLETING FORM

(Additional pages may be attached if more space is needed.)

### GENERAL

- Use a separate form for each patient. Complete the form to the best of your abilities. Items 3, 4, 7, 8, 10, 11, and 13 are considered essential and should be completed whenever possible. Parents/Guardians may need to consult the facility where the vaccine was administered for some of the information (such as manufacturer, lot number or laboratory data.)
- Refer to the Reportable Events Table (RET) for events mandated for reporting by law. Reporting for other serious events felt to be related but not on the RET is encouraged.
- Health care providers other than the vaccine administrator (VA) treating a patient for a suspected adverse event should notify the VA and provide the information about the adverse event to allow the VA to complete the form to meet the VA's legal responsibility.
- These data will be used to increase understanding of adverse events following vaccination and will become part of CDC Privacy Act System 09-20-0136, "Epidemiologic Studies and Surveillance of Disease Problems". Information identifying the person who received the vaccine or that person's legal representative will not be made available to the public, but may be available to the vaccinee or legal representative.
- Postage will be paid by addressee. Forms may be photocopied (must be front & back on same sheet).

### SPECIFIC INSTRUCTIONS

Form Completed By: To be used by parents/guardians, vaccine manufacturers/distributors, vaccine administrators, and/or the person completing the form on behalf of the patient or the health professional who administered the vaccine.

Item 7: Describe the suspected adverse event. Such things as temperature, local and general signs and symptoms, time course, duration of symptoms diagnosis, treatment and recovery should be noted.

Item 9: Check "YES" if the patient's health condition is the same as it was prior to the vaccine, "NO" if the patient has not returned to the pre-vaccination state of health, or "UNKNOWN" if the patient's condition is not known.

Item 10 and 11: Give dates and times as specifically as you can remember. If you do not know the exact time, please indicate "AM" or "PM" when possible if this information is known. If more than one adverse event, give the onset date and time for the most serious event.

Item 12: Include "negative" or "normal" results of any relevant tests performed as well as abnormal findings.

Item 13: List ONLY those vaccines given on the day listed in Item 10.

Item 14: List any other vaccines that the patient received within 4 weeks prior to the date listed in Item 10.

Item 16: This section refers to how the person who gave the vaccine purchased it, not to the patient's insurance.

Item 17: List any prescription or nonprescription medications the patient was taking when the vaccine(s) was given.

Item 18: List any short term illnesses the patient had on the date the vaccine(s) was given (i.e., cold, flu, ear infection).

Item 19: List any pre-existing physician-diagnosed allergies, birth defects, medical conditions (including developmental and/or neurologic disorders) for the patient.

Item 21: List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations. If more than one brother or sister, or if the patient has reacted to more than one prior vaccine, use additional pages to explain completely. For the onset age of a patient, provide the age in months if less than two years old.

Item 26: This space is for manufacturers' use only.

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## CONTINUING MEDICAL EDUCATION (CME) QUESTIONS & ANSWERS

**1. Which of the following is NOT a known limitation of pre-marketing clinical trials?**

A. Ability to detect common adverse reactions.
B. Small study size.
C. Short study duration.
D. Narrow set of indications.
E. Evaluates diverse populations.

**2. Which of the following statements is TRUE?**

A. Post-marketing passive surveillance is conducted under controlled conditions in defined populations.
B. The ability to detect adverse events after vaccination is enhanced with the routine use of multiple vaccines.
C. Adverse event detection relies on accurate reporting from health care providers.
D. The number of doses of vaccine administered to the public is accessible to the public.
E. Once a vaccine is marketed, its initial/product information does not change.

**3. All of the following are known limitations of passive surveillance systems based on spontaneous reports EXCEPT:**

A. Includes the entire U.S. population.
B. Under-reporting.
C. Bias.
D. Lack of consistent diagnostic criteria for disease.
E. Lack of denominator data.

**4. All of the following are known strengths of spontaneous (passive) surveillance systems based on spontaneous reports EXCEPT:**

A. Cost-effective in detecting rare, serious adverse events.
B. Hypothesis generation (identification of a signal).
C. Studies geographically diverse population.
D. Relatively immune to bias.
E. Large portion of voluntary reports from conscientious, astute health professionals.

**5. Which of the following statements is FALSE with regard to VAERS?**

A. An event that is life-threatening or requires hospitalization or prolonged hospitalization, or permanent disability is considered serious.
B. An event must be causally related to vaccine to be reported to VAERS
C. VAERS can assess the safety of specific vaccine lots.
D. Manufacturers are required to report serious adverse events to VAERS.
E. The identity of the vaccinee is kept confidential.

**6. Objectives of VAERS includes all of the following EXCEPT:**

A. Identification of increased rates of known side effects.
B. Identification of risk factor that may promote disease.
C. Identification of new, rare vaccine reactions.
D. Assessment of vaccine lot safety.
E. Conduct of controlled studies to determine if an event was caused by the vaccine.

**7. Which of the following is FALSE?**

A. Careful consideration of the limitations of VAERS is relevant to accurate interpretation of VAERS data.
B. A large number of VAERS events cannot be interpreted as clear-cut evidence that an event is causally related to vaccination.
C. Biological plausibility and strength of association are very important in adverse event report evaluation.
D. It is possible to interpret VAERS data without knowing the number of persons who were vaccinated ("denominator" data).
E. Follow-up epidemiologic investigations may stem from identification of unusual VAERS reports.

**8. All of the following are FDA actions that can result from careful analysis of spontaneous adverse event reports EXCEPT:**

A. Requesting manufacturer-sponsored post-marketing studies.
B. Requiring manufacturer to compensate for damages suffered because of a vaccine-related adverse event.
C. Change in label/product information.
D. Working with manufacturer on the issuance of a Safety Alert that outlines the serious safety issue involved.
E. Recalling a vaccine lot.

**9. All of the following are methods by which the FDA disseminates vaccine safety-related information to health care providers EXCEPT:**

A. Publications in scientific literature.
B. Presentations at public forums.
C. VAERS Website on the internet.
D. Work with manufacturers on the issuance of "Dear Health Professional" letters.
E. None of the above -- ALL are used by the FDA to inform health care providers of new safety information.

**10. The effectiveness of VAERS is dependent on all of the following EXCEPT:**

A. Active participation of health professionals to report vaccine-associated events to VAERS.
B. Adequately financing the high costs needed to maintain VAERS.
C. Careful consideration of the limitations of VAERS while interpreting data.
D. Ensuring confidentiality against disclosure of patient identifies.
E. Filing of complete VAERS reports including clinical diagnosis and details of the course of events.

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**Post-Marketing Surveillance: VAERS**

# MEDWATCH

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| | |
|---|---|
| The information presented is relevant to my clinical practice | _____Y _____N |
| **1.** Was the material new for you? | _____Y _____N |
| **2.** Was the material presented clearly? | _____Y _____N |
| **3.** Was the material covered adequately? | _____Y _____N |
| **4.** Can you explain the importance of vaccine post-marketing surveillance? | _____Y _____N |
| **5.** Are you able to define your responsibility to report adverse events? | _____Y _____N |
| **6.** Are you able to discuss basic limitations and strengths of VAERS? | _____Y _____N |
| **7.** Do you understand the objectives of VAERS? | _____Y _____N |
| **8.** Are you able to describe ways in which FDA informs health professionals about vaccine safety? | _____Y _____N |
| **9.** Are you able to describe what impact post-marketing passive surveillance systems have on your clinical practice? | _____Y _____N |
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Suggested Topics: _____

**Mail the completed answer sheet by 10/31/01 to:**
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**DEPARTMENT OF
HEALTH & HUMAN SERVICES**

Public Health Service
Food and Drug Administration, HF-2
Rockville, MD 20857 USA



**VAERS**

**THE FDA/CDC VACCINE ADVERSE EVENT REPORTING SYSTEM**

www.fda.gov/cber/vaers.html

# Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS)

Complimentary CE Article

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