

Tracking Vaccine-Safety Inquiries to Detect Signals and Monitor Public Concerns

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KEY WORDS

public inquiries, vaccine safety, vaccine adverse events

ABBREVIATIONS

AE—adverse event

VAERS—Vaccine Adverse Event Reporting System

CDC—Centers for Disease Control and Prevention

CISA—Clinical Immunization Safety Assessment

ISO—Immunization Safety Office

ITS—Inquiry Tracking System

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abstract

BACKGROUND: The Centers for Disease Control and Prevention frequently receives inquiries from health care providers, public health officials, and the general public seeking data or guidance on vaccine-safety issues. Past inquiries to public health authorities identified potential problems including viscerotropic illness rarely associated with yellow fever vaccination.

OBJECTIVE: To systematically describe vaccine-safety inquiries received at the Centers for Disease Control and Prevention.

METHODS: External and internal inquiries were recorded in a database from May 1, 2002 to May 31, 2009. Key variables analyzed included the source of the question, the type of information being sought, and the vaccine type(s) associated with the inquiry.

RESULTS: A total of 983 vaccine-safety inquiries were answered and analyzed. Health care workers were the source of 43% of the questions, and the general public accounted for 19% of the questions. Nearly half of the requests (49%) concerned information about the Vaccine Adverse Event Reporting System, and nearly one-fourth (21%) were requests from providers for clinical guidance. The most frequent specific topics of inquiry and vaccines involved were neurologic adverse events (AEs) temporally associated with vaccination (17%) and safety of all vaccines or childhood vaccines (20%), respectively.

CONCLUSIONS: Questions about rare but potentially serious AEs and general concerns about vaccine safety were encountered relatively frequently. The substantial number of clinically focused inquiries may indicate a need for more provider support tools and resources. Tracking of inquiries can supplement information received through vaccine AE reporting and contribute to an enhanced scientific and communications response to vaccine-safety concerns. *Pediatrics* 2011;127:S87–S91

As vaccination-coverage rates increase and the incidence of vaccine-preventable disease decreases, the number of reported adverse events (AEs) temporally associated with vaccines increases. In addition, public concern for AEs also tends to increase.¹ In addition to reducing the burden of vaccine-related injury, close attention to vaccine safety helps secure public support for vaccination programs and helps to increase uptake of vaccinations.^{2,3}

The Vaccine Adverse Event Reporting System (VAERS) is a federally mandated passive surveillance system that accepts reports of AEs that have a temporal association with US-licensed vaccines.¹ VAERS accepts reports from the United States and elsewhere. It is managed by the Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration. VAERS plays a central role in detecting “signals” for vaccine-safety problems that require further investigation by means of more systematic studies. However, VAERS has a number of limitations including underreporting.^{1,4–6} Most of the (AE) reports are voluntary and depend on potential reporters’ recognizing that a problem may be vaccine related, which is often not an easy task.⁷ Underreporting limits our ability to analyze and detect possible associations between vaccines and AEs. Failure to fully capture cases can cause potential indications of previously unknown side effects to be missed.^{8,9} In addition, more common AEs may be undercounted. Serious AEs are more likely to be reported than those that are less serious, but reporting of any AE depends, in large part, on alert health care providers.^{7,9} Serious AEs are defined by the Food and Drug Administration as those that result in death, life-threatening illness, hospitalization, prolongation of an existing hospitalization, or permanent disability.

In addition to VAERS reporting, the CDC uses several other methods to study vaccine safety, including the Vaccine Safety Datalink and the Clinical Immunization Safety Assessment (CISA) Network. These activities reside in the CDC Immunization Safety Office (ISO) and have been described elsewhere.^{10,11} Briefly, the Vaccine Safety Datalink is a collaborative effort between the CDC ISO and 8 large linked databases to monitor vaccine safety by performing population studies that use data from electronic medical records. The CISA Network is a collaborative effort between the CDC ISO and 6 medical research centers to conduct clinical research on vaccine AEs on the individual patient level.

Inquires to federal agencies prompted investigations into possible links between vaccines and health problems before the start of the Inquiry Tracking System (ITS), including recognition of viscerotropic illness associated with yellow fever vaccine¹² (which led to enhanced surveillance for AEs after yellow fever vaccine, dissemination of information to certified yellow fever vaccination centers, and a label change for the yellow fever vaccine) and the possible association of alopecia with the hepatitis B vaccine.¹³

In May 2002, the CDC ISO developed the ITS to systematically monitor all the inquiries it received to augment reporting to VAERS, to identify issues that need further investigation, and to detect emerging trends in vaccine-safety concerns. In this report we describe the initial results of the CDC ITS.

METHODS

The CDC ISO receives inquiries from a variety of sources. The 2 primary sources of immunization-related inquiries are the CDC telephone information line (1-800-CDC-INFO/1-800-232-4636) and the CDC vaccine e-mail account (nipinfo@cdc.gov [NIPINFO is the com-

monly used term for the National Immunization Program e-mail account]).^{14,15} The CDC telephone hotline is an integrated information line through which callers can ask questions on any health topic including immunization. The staffers on this hotline have access to information prepared by CDC immunization experts. In addition, health care providers who staff this hotline are also available to answer the more complex or unusual types of questions. The CDC NIPINFO e-mail account, staffed by physicians, nurses, and health education specialists who are experts in the immunization field, answer immunization questions by e-mail from both laypersons and health care professionals. Vaccine-safety questions that cannot be answered by staff members of these services are often referred to ISO staff—physicians, nurses, and epidemiologists who are experts in the field of vaccine safety. They have direct access to VAERS and other sources of safety data. The ISO also receives questions, usually via e-mail, from a variety of other sources (see Fig 1).

An Access (Microsoft, Redmond, WA) database is used to record inquiries that reach the ISO. Questions are recorded in their entirety and then categorized according to source, mode of communication, and general topic of the question and according to vaccine or AE. Responses to inquiries are also recorded in their entirety. Questions about AEs prompt searches for similar previous queries to both detect patterns and prepare consistent responses. ISO staff members were requested to copy all responses to 1 staff member who was responsible for recording the information in the ITS. We analyzed all inquiries received between May 1, 2002, and May 31, 2009, for the reason for the inquiry, inquiry subject, vaccine in question, and inquiry source. Follow-up data for clini-

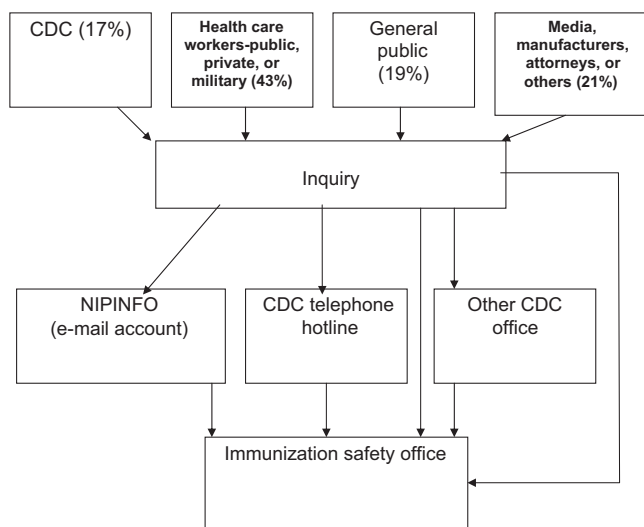


FIGURE 1 Inquiry sources and information flow diagram for the CDC ISO from May 2002 to March 2007.

cal outcome or understanding of response were not routinely collected.

RESULTS

The ISO responded to 983 inquiries between May 2002 and May 2009 (~11 per month). Health care workers (public, private, or military) submitted 419 queries (43%), members of the general public submitted 185 (19%), and staff from other areas of the CDC submitted 172 (17%). Staff of NIPINFO sent 142 (14%) inquiries to the ISO, and those who were manning the CDC telephone information line sent 121 (12%).

During the same time period, VAERS received a total of 142 995 US reports (data not shown), and the NIP e-mail account addressed ~25 to 39 inquiries per day, of which ~4% to 5% were related to vaccine-safety issues (NIPINFO staff, personal communications, June 29, 2009). During this time period, 142 inquiries were forwarded to the ISO from NIPINFO, which accounts for a small fraction of vaccine-safety inquiries to NIPINFO.

The 3 main reasons the ISO was contacted were to (1) obtain information regarding VAERS data (49%), (2) obtain

clinical or medical advice (21%), and (3) obtain general vaccine-related information (11%) (see Table 1). Topics discussed most often included (1) neurologic AEs possibly associated with vaccination, such as encephalomyelitis, Bell’s palsy, brachial neuritis, and Guillain-Barré syndrome (168 questions [17%]) and their potential relationship with vaccination, (2) deaths (including sudden infant death syndrome) that had a temporal association to vaccines (77 questions [8%]), (3) injection-site reactions after vaccination, including cellulitis, pain at the injection site, and whole-limb swelling (60 questions [6%]), (4) general VAERS data requests (57 questions [6%]), and (5) allergic reactions including rash or serum sickness (54 questions [5%]) (see Table 1).

All vaccines or childhood vaccines were most frequently mentioned in the inquiries (224 queries [20%]), followed by diphtheria, tetanus, and/or pertussis-containing vaccines (154 queries [14%]). Queries about influenza vaccines accounted for 149 (13%) and human papilloma virus vaccines accounted for 74 (7%) of the questions (see Table 1).

TABLE 1 Summary Statistics on the ITS for the CDC ISO From May 1, 2002, to May 31, 2009

Reason for Inquiry	n (%) ^a
VAERS data (N = 975)	482 (49)
Clinical/medical advice	200 (21)
General vaccine information	107 (11)
VAERS reporting/process	55 (6)
Vaccine-specific questions	53 (5)
Data request not answered by the VAERS	38 (4)
Vaccine lot-number searches in the VAERS	22 (2)
Support for vaccine AE	16 (2)
Other	2 (0)
Inquiry subject (N = 983)	
Neurologic topics	168 (17)
Death/sudden infant death syndrome	77 (8)
Injection-site reactions	60 (6)
VAERS data requests	57 (6)
Allergic reactions/rash/serum sickness/hypersensitivity	54 (5)
Vaccine-administration techniques/errors	28 (3)
Contraindications/revaccination issues	25 (3)
Autism/thimerosal	23 (2)
Other	495 (50)
Vaccines most frequently discussed (N = 1121)	
All vaccines or all childhood vaccines	224 (20)
Diphtheria, tetanus, and/or pertussis	154 (14)
Influenza	149 (13)
Human papilloma virus	74 (7)
Hepatitis B	66 (6)
Measles, mumps, and/or rubella	62 (6)
Yellow fever	61 (5)
Varicella	54 (5)
Anthrax	46 (4)
Other	231 (21)
Inquiry source (N = 983)	
Health care providers (public, private, or military)	419 (43)
General public	185 (19)
CDC	172 (17)
Media	29 (3)
Vaccine manufacturers	26 (3)
Attorneys	22 (2)
Other	130 (13)

^a All percentages are rounded to the nearest whole number. More than 1 vaccine or subject can be associated with 1 inquiry. Percentages may not add up to 100 because of rounding.

DISCUSSION

By maintaining a record of inquiries, CDC staff members have been better able to stay informed of issues that concern the public and providers,

which has been helpful in determining educational content on CDC vaccine-safety information Web sites. The data collected from the ITS influence ISO messages and outreach. Because requestors ask more questions about neurologic AEs than about any other topic, the ISO staff members are planning to include a section dedicated to this topic on their Web site.

The questions received by the ISO are varied and include requests for VAERS data searches, information about the Vaccine Injury Compensation Fund, general information on vaccine safety, and medical advice. Although CDC staff members do not provide medical advice to patients, they refer select provider questions to the CISA Network. CISA Network principal investigators have extensive clinical expertise in vaccine safety and have developed study protocols for certain AEs (eg, Guillain-Barré syndrome after vaccination and revaccination for persons with previous hypersensitivity reaction after vaccination).

For cases in which requestors discussed an AE after vaccination that was not reported to VAERS, CDC staff members requested them to file a VAERS report. If the requestor was not familiar with how to file the report, the CDC staff member provided information and/or assistance.

Vaccine-safety inquiries are not only addressed to the ISO. State and local health departments, primary care providers, and CDC information telephone lines and e-mail services are all involved in responding to vaccine-safety inquiries. In general, these other health organizations likely refer inquiries to the ISO that they are not capable of answering themselves, which could be because of the complex nature of the questions or because these organizations do not have data that are needed to answer a request. This selective referral in-

troduces a bias into the inquiries received, but it does not detract from the usefulness of the ITS as a supplement to the VAERS, the Vaccine Safety Datalink, and the CISA Network for the purpose of identifying new potential safety concerns or signals of potential adverse reactions.

The ITS has shown several interesting trends in monitoring public vaccine-safety concerns. Inquiries for VAERS data account for nearly half of all requests, and questions on neurologic problems account for ~17% of inquiries. The requests for VAERS data reflect the CDC's and Food and Drug Administration's role in managing VAERS. Although these data have been available on the VAERS Web site to download for the last several years, analysis of the data required programming skills that the layperson does not have. Since September 2006, a search tool that is much simpler to use and does not require programming skills is now available on the VAERS Web site (www.vaers.hhs.gov).

The inquiries about neurologic AEs most likely reflect the public's interest in AEs that result in hospitalization, disability, or death and AEs with etiologies that are not clearly understood, even if these AEs are rare (eg, Guillain-Barré Syndrome after the meningococcal vaccine).

Health care and public health workers are probably more likely to know of or be referred to the ISO, which is indicated by the highest number of questions from these groups.

The CDC maintains Web sites aimed at both the lay public and health care professionals for the purpose of health education and information. The CDC's ISO Web site (www.cdc.gov/vaccinesafety/index.html) focuses specifically on health education and risk communication related to vaccine-safety issues. One goal of the ITS is to help determine what fre-

quently asked questions and questions and answers will be posted on the ISO Web site and will be available to the public and media. For example, the questions on sudden infant death syndrome and autism are on the site because of the public's interest in these topics. ITS analysis can help to ensure that the public is provided vaccine-safety information that is harmonized across federal agencies, manufacturers, clinicians, and state health departments.

LIMITATIONS

The ITS has several limitations. The sample of recorded safety-related inquiries is quite small compared with other more commonly used systems for inquiries, such as NIPINFO. ITS inquiries are biased toward complex questions. In addition, because relatively few questions are referred to the ISO from the CDC telephone information service or NIPINFO, most questions are probably answered before they reach the ISO and, therefore, are not recorded in the ITS. As a result, the recorded inquiries may not be representative of vaccine-safety-related concerns that are asked about most frequently. For example, autism, possibly the most publicly discussed topic in vaccine safety, was the subject of only 2% of questions in the ITS, because staff members of 1-800-CDC-INFO and NIPINFO answer autism questions before they reach the ISO. In addition, many requests could fall into more than 1 category, because the analyzed groupings are not always mutually exclusive.

CONCLUSIONS

Despite limitations, tracking vaccination inquiries has been useful. The ITS is an additional system in which to look for previously unreported AEs. It has enabled ISO staff to be more aware of vaccine-safety issues

about which the public has concerns and is a resource for questions that are asked frequently. Other public health organizations should consider recording the inquiries they receive about vaccinations. Keeping

records of inquiries and associated responses will help public health workers address common questions, respond to these inquiries in a consistent manner, and remain cognizant of vaccine-safety concerns of

both laypersons and health care professionals.

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