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CDC did not accept commercial support for this continuing education activity.
Updates from CDC’s Immunization Safety Office (CDC-ISO): What Public Health Officials and Health Care Providers Need to Know

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Theresa Harrington, MD, MPH
Immunization Safety Office
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases

National Immunization Conference
May 16, 2018
Disclaimer

- Findings and conclusions in this presentation are those of the presenters and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC)
- Use of product trade name is for identification purposes only
Vaccine Adverse Event Reporting System
Outline

- Background
- Overview of CDC’s Immunization Safety Office (ISO)
- Vaccine Adverse Event Reporting System (VAERS)
- ISO inquiry response
Vaccine safety path

Before licensure
- Lab research
- Animal studies
- Studies in people

After licensure
- Safety monitoring and studies especially for events too rare to be detected in pre-licensure studies
- Guidelines and education

FDA* licensure
- Vaccine is safe & effective
- Vaccine can be made safely

*Food & Drug Administration
What is a vaccine adverse event?

- Any untoward medical occurrence following vaccination*
- Does not necessarily have a causal relationship with vaccination
- May be any unfavorable or unintended condition
  - Sign
  - Symptom
  - Abnormal laboratory finding
  - Disease

CDC’s Immunization Safety Office (ISO) mission

- Assess the safety of vaccines given to children, adolescents and adults
  - Post-licensure surveillance to detect possible adverse events (AEs) following vaccination in a timely way
  - Assessment of strategies for prevention of AEs following vaccination
  - Vaccine safety research
  - Timely communication and education to partners and public
- Work with other federal agencies and other organizations to further vaccine safety mission
ISO’s post-licensure vaccine safety monitoring infrastructure

<table>
<thead>
<tr>
<th>System</th>
<th>Collaboration</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Adverse Event Reporting System (VAERS)</td>
<td>CDC and FDA</td>
<td>US frontline spontaneous reporting system to detect potential vaccine safety problems</td>
</tr>
<tr>
<td>Vaccine Safety Datalink (VSD)</td>
<td>CDC and healthcare plans</td>
<td>Large linked database system used for active surveillance and research</td>
</tr>
<tr>
<td>Clinical Immunization Safety Assessment (CISA) Project</td>
<td>CDC and medical research centers</td>
<td>Expert collaboration which conducts individual clinical vaccine safety assessments and clinical research</td>
</tr>
</tbody>
</table>
Vaccine Adverse Event Reporting System (VAERS)

- National spontaneous (or passive) reporting system for AEs after US-licensed vaccines
  - Receives ~40,000 reports annually*
  - Accepts reports from healthcare providers, manufacturers and public
  - Signs/symptoms of AE are coded using the Medical Dictionary for Regulatory Activities (MedDRA)± terms and entered into a database
  - Primarily used for signal detection and hypothesis generation
- Jointly administered by CDC and FDA since 1990

*2012-2016
±http://www.meddra.org/
### VAERS strengths and limitations

<table>
<thead>
<tr>
<th><strong>Strengths</strong></th>
<th><strong>Limitations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Rapid signal detection</td>
<td>• Reporting bias</td>
</tr>
<tr>
<td>• Can detect rare AEs</td>
<td>• Inconsistent data quality and completeness</td>
</tr>
<tr>
<td>• Collects information about vaccine, characteristics of vaccinee, AE</td>
<td>• Lack of unvaccinated comparison group</td>
</tr>
<tr>
<td>• Data available to public</td>
<td>• Generally cannot assess if vaccine caused an AE</td>
</tr>
</tbody>
</table>
What to report to VAERS*

- Medically important health event/AE following vaccination
  - Local: redness, swelling, pain at injection site
  - Systemic: fever, myalgia, headache
  - Allergic: hives, pruritis, anaphylaxis
  - Vaccination errors (e.g., wrong drug administered)

- National Childhood Vaccine Injury Act mandates health care providers report specific AEs following vaccination
  - VAERS Table of Reportable Events
    - https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf

*https://vaers.hhs.gov/
VAERS form: information collected

- Patient, provider and reporter demographics, AEs, vaccines, preexisting conditions
- Date vaccinated, vaccine type, lot number, dose number
- Reports with incomplete information accepted
- All reports accepted without judgment on causality
- Report as soon as possible (no time limit on reporting)
VAERS follow-up

- VAERS staff follow up with health care providers on serious* reports
  - Medical records
  - Death certificates/autopsy reports
- FDA and CDC review medical records and VAERS reports for serious reports

*Based on the Code of Federal Regulations
Reporting using VAERS form

- Submit reports by
  - Direct online reporting – use VAERS online reporting tool
  - Download and complete fillable and savable VAERS form – use electronic document upload feature
Have you had a reaction following a vaccination?

1. Contact your healthcare provider.
2. Report an Adverse Event using the VAERS online form or the new downloadable PDF. [New]

Important: If you are experiencing a medical emergency, seek immediate assistance from a healthcare provider or call 9-1-1. CDC and FDA do not provide individual medical treatment, advice, or diagnostics. If you need individual medical or healthcare advice, consult a qualified healthcare provider.

¿Ha tenido una reacción después de recibir una vacuna?

1. Contacte a su proveedor de salud.
2. Reporte una reacción adversa utilizando el formulario de VAERS en línea o la nueva versión PDF descargable. [Nuevo]
CDC’s Immunization Safety Office
Inquiry Response
Immunization Safety Office (ISO) inquiry response

- ISO has staff on call for 365 days a year for vaccine safety inquiries

Sources of vaccine safety inquiries to ISO

- Healthcare providers, health officials from state and local health departments and the general public send inquiries to CDC through
  - CDC Info: CDCINFO@cdc.gov
  - NIP Info: NIPINFO@cdc.gov
  - VAERS mailbox: Info@VAERS.org
  - CDC Emergency Operations Center (EOC)
  - Directly to ISO staff

- Healthcare providers can send requests for CISA consults through
  - CISA site: CISAeval@cdc.gov
Resources ISO uses to answer questions on vaccine safety topics

- **Vaccine Adverse Event Reporting System (VAERS)**
  - Data searches

- **Vaccine Safety Datalink (VSD)**

- **Clinical Immunization Safety Assessment (CISA) Project**
  - Request for consults from healthcare providers via email to CISAeval@cdc.gov
Resources ISO uses to answer questions on vaccine safety topics (cont.)

- Vaccine package inserts
  - [http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm](http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm)
Resources ISO uses to answer questions on vaccine safety topics (cont.)

- Advisory Committee on Immunization Practices (ACIP) Guidelines
  - [https://www.cdc.gov/vaccines/hcp/acip-recs/index.html](https://www.cdc.gov/vaccines/hcp/acip-recs/index.html)
Resources ISO uses to answer questions on vaccine safety topics (cont.)

- National Academy of Medicine (formerly Institute of Medicine) review: Adverse Effects of Vaccines

- Published studies from peer reviewed journals
  - Pub Med search

- CDC Subject Matter Experts
Example of a question

- My wife had a stroke less than 24 hours after she received a flu shot. Have there been any reports of such an adverse reaction to a flu shot?
Example of a response

- Although there are case reports of stroke after flu vaccine, flu vaccines do not cause strokes.
- Published literature does not support an increased risk of stroke following influenza vaccination.
- Study in the journal Vaccine in 2015: Risk of stroke was reduced in the 59 days following influenza vaccination in >17,000 persons.
- American Stroke Association recommends annual flu vaccination for patients at risk of stroke.
Example of a question

- Have any adverse events been reported following inadvertent adjuvant reconstitution using sterile water rather than the diluent supplied by the manufacturer for Shingrix®?
Example of a response

- We have no reports of Shingrix® being given with sterile water rather than the diluent supplied by the manufacturer. For incorrect reconstitution the dose is invalid but the recovery dose may be administered as soon as possible.
- Take necessary steps to help train staff to prevent future vaccination errors.
- CDC training webcasts on this topic at https://www.cdc.gov/vaccines/hcp/admin/resource-library.html
Reconstitution of adjuvanted recombinant zoster vaccine

CDC postings on vaccine safety issues
For vaccination questions

- Call 1-800-CDC-INFO
- Email Nipinfo@cdc.gov
Acknowledgements

- CDC
  - Elaine Miller
  - Tiffany Suragh

- FDA
Overview of CDC’s Clinical Immunization Safety Assessment (CISA) Project
Clinical Consultation Service
Overview

- Overview of Clinical Immunization Safety Assessment (CISA) Project
- CISA clinical consultation processes
- CISA published example cases
<table>
<thead>
<tr>
<th>CISAProject Site</th>
<th>Principal and Senior Investigators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boston Medical Center, MA</td>
<td>Elizabeth Barnett, MD</td>
</tr>
<tr>
<td></td>
<td>Stephen Pelton, MD</td>
</tr>
<tr>
<td>Cincinnati Children’s Hospital Medical Center, OH</td>
<td>Steven Black, MD</td>
</tr>
<tr>
<td></td>
<td>Elizabeth Schlaudecker, MD, MPH</td>
</tr>
<tr>
<td></td>
<td>Mary Staat, MD, MPH</td>
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<tr>
<td>Columbia University, NY</td>
<td>Anne Gershon, MD</td>
</tr>
<tr>
<td></td>
<td>Philip LaRossa, MD</td>
</tr>
<tr>
<td></td>
<td>Melissa Stockwell, MD, MPH</td>
</tr>
<tr>
<td>Duke University, NC</td>
<td>Emmanuel “Chip” Walter, MD, MPH</td>
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<tr>
<td></td>
<td>Geeta Swamy, MD</td>
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<tr>
<td></td>
<td>Ken Schmader, MD</td>
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<tr>
<td>Johns Hopkins University, MD</td>
<td>Neal Halsey MD</td>
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<td></td>
<td>Kawsar Talaat, MD</td>
</tr>
<tr>
<td>Kaiser Permanente Northern California, CA</td>
<td>Nicola Klein, MD, PhD</td>
</tr>
<tr>
<td>Vanderbilt University Medical Center, TN</td>
<td>Kathryn M. Edwards, MD</td>
</tr>
<tr>
<td></td>
<td>Buddy Creech, MD, MPH</td>
</tr>
</tbody>
</table>
Clinical Immunization Safety Assessment (CISA) Project*

- **Mission**
  - To improve understanding of adverse events after following immunization (AEFI) at the individual level

- **Goals**
  - To serve as vaccine safety resource for U.S. healthcare providers with complex vaccine safety questions about a specific patient to assist with immunization decision-making
    - Advice from CDC and CISA is meant to assist in decision-making rather than provide direct patient management. Patient management decisions are the responsibility of the treating healthcare provider
  - To conduct clinical research studies to better understand vaccine safety and identify preventive strategies for AEFI
  - To assist the Centers for Disease Control and Prevention (CDC) and its partners evaluating emerging vaccine safety issues

*CISA network started 2001; new 10-year contract started in 2012
Requesting a CISA consultation

CISA Evaluation

CISAeval@cdc.gov

If you are a US healthcare provider with a vaccine safety question about a specific patient residing in the US that is not readily answered by Advisory Committee on Immunization Practices (ACIP) guidelines and you seek expert opinion, you can contact CDC to request a CISA evaluation. This service is provided free of charge.
CISA clinical consultation process
Step 1: Submitting request for consultation

▪ US-licensed healthcare provider has a vaccine safety question about an individual patient
  - Adverse event(s) following immunization (AEFI) and guidance for future vaccine(s)
  - Question about possible risk of an AEFI given patient or family history

▪ Question not readily answered by local specialists or resources, Advisory Committee on Immunization Practices (ACIP) guidance, or other professional society guidance (e.g., AAP, ACOG, IDSA)

▪ Healthcare provider submits request (CISA website): CISAeval@cdc.gov

CISA clinical consultation process
Step 2: CISA medical officer contacts provider

- Review case and confirm need for consultation
  - If inquiry is not a good fit for CISA consultation, it will be routed to appropriate groups within CDC for a response
- Review healthcare provider’s roles and responsibilities
  - Provider facilitates collection of medical records
  - Provider responds to post-consultation surveys
- Review privacy/confidentiality regulations
- Assess timeline for scheduling consultation
  - Usually needs 2-4 weeks to collect medical records and prepare case; urgent consultations can be accommodated
- Schedule consultation (Full vs. Mini)
- Provider is encouraged to submit report to VAERS
CISA clinical consultation process
Step 3: CISA case preparation

- CISA subject matter experts (SMEs) summarize
  - Medical records (progress notes, lab and imaging reports, vaccine records)
  - Pertinent medical/scientific literature (English language)
  - VAERS analyses of similar AEFI reports
  - FDA/manufacturer package insert information
  - Immunology and pathophysiology of AEFI (if known)
  - Institute of Medicine (IOM) reports on vaccine adverse event causality*
  - HRSA Vaccine Injury Table**
  - Case-centered analyses may be included***

FDA: U.S. Food and Drug Administration; HRSA: Health Resources and Services Administration; DoD: Department of Defense

*IOM is now National Academy of Medicine; www.nationalacademies.org/hmd/Global/Topics/Vaccines.aspx

**https://www.hrsa.gov/vaccine-compensation/index.html

Additional consultation call preparation

- All attendees on the call must sign Assurance of Confidentiality
  - Healthcare provider who requested the consultation
  - CISA site SMEs, CDC SMEs, federal partners (FDA, HRSA, DoD)
- Patients and parents of patients, even if they are healthcare providers, are not invited to join the call
  - They may provide photos, diaries to healthcare provider to share with CISA

SMEs: Subject matter experts; FDA: U.S. Food and Drug Administration; HRSA: Health Resources and Services Administration; DoD: Department of Defense
CISA clinical consultation process
Step 4: case presentation and discussion

- CISA SMEs present and discuss all information prepared for the case ("Grand Rounds" format)
  - Clinical and laboratory data
  - Pathophysiology and immunology of AEFI
  - Assess biologic plausibility of AEFI with respect to vaccine(s)

- Questions are addressed
  - Healthcare provider is encouraged to ask questions
  - Verbal guidance is shared regarding future vaccines for patient and any additional testing that might be indicated

- Assessment of causality performed for AEFIs using algorithm*

Algorithm to assess causality after AEFI

CISA clinical consultation process
Step 5: CISA post-consultation processes

- CISA provides post-consultation guidance letter
  - Summarizes pertinent consult information and guidance
  - Can be added to patient medical record and shared with patient/family

- Two surveys are sent to healthcare provider
  - ‘Satisfaction’ survey (<2 weeks after consultation)
    - Ask provider to assess consultation experience
  - Patient ‘outcome’ survey (weeks to months after consultation)
    - Document patient outcome (AEFI or not) after receipt of future vaccine(s)
    - Assess adherence to CISA guidance
    - Collect provider impression of quality and usefulness of CISA guidance

- Consultation and follow-up information entered into secure database
  - Assist CDC-ISO with tracking clinical outcomes after vaccine safety consultations
  - Help provide future vaccine safety guidance

*Research Electronic Data Capture (REDCap); https://www.project-redcap.org/*
# CISA clinical case consultations

<table>
<thead>
<tr>
<th></th>
<th>Years 1-6 (Oct 2012 - Jan 2018)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of cases reviewed</strong></td>
<td>114 unique cases*</td>
</tr>
<tr>
<td><strong>Evaluated AEFI and provided guidance</strong></td>
<td>98 (86%)</td>
</tr>
<tr>
<td><strong>Guidance only, no AEFI</strong></td>
<td>16 (14%)</td>
</tr>
<tr>
<td><strong>Median/mean age of patient at time of consultation (range)</strong></td>
<td>5.0 yrs/12.9 yrs (in utero – 72 yrs)</td>
</tr>
<tr>
<td><strong>Influenza vaccine involved</strong></td>
<td>44 cases (38.6%)</td>
</tr>
</tbody>
</table>

*Some case require multiple consultation calls to gather additional data
## Causality algorithm* assessment (Oct 2012-Jan 2018)

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Total (N=114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inconsistent with</td>
<td>16 (14%)</td>
</tr>
<tr>
<td>Consistent with</td>
<td>21 (18%)</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>60 (53%)</td>
</tr>
<tr>
<td>Not applicable (No AEFI, guidance-only case)</td>
<td>13 (11%)</td>
</tr>
<tr>
<td>Causality assessment pending final determination</td>
<td>4 (4%)</td>
</tr>
</tbody>
</table>

Example consultations

- Concern that AEFI might occur due to patient history
  - Severe Stevens-Johnson syndrome (SJS) after wild type influenza B infection
    Should child receive influenza vaccine this influenza season?

- AEFI case
  - Sudden sensorineural hearing loss after seasonal influenza vaccine
Example 1: non-AEFI consultation

Influenza B virus infection and Stevens–Johnson syndrome

Rebecca L. Tamez MD¹ | Whitney V. Tan MD² | John T. O'Malley MD, PhD³ |
Karen R. Broder MD⁴ | Maria C. Garzon MD²,⁵ | Philip LaRussa MD⁵ |
Christine T. Lauren MD²,⁵

Abstract
A 2-year-old boy with influenza B infection and rapidly worsening targetoid skin lesions with mucosal involvement was diagnosed with Stevens–Johnson syndrome (SJS) and treated with oseltamivir and intravenous immunoglobulin, with resolution of illness. Subsequent quadrivalent inactivated influenza vaccine was well tolerated. This case highlights the rarity of SJS in the setting of influenza B infection and addresses the safety of administering subsequent influenza vaccines to such individuals.

Keywords
influenza vaccine, intravenous immunoglobulin, vaccine safety
Stevens-Johnson Syndrome (SJS) after influenza B infection

- 2 y/o healthy male child was hospitalized in intensive care for severe SJS involving >10% body surface area
  - Influenza B virus was the only pathogen identified
- 8 months later, the child has recovered and is doing well
- Child’s influenza immunization history
  - Tolerated trivalent inactivated influenza vaccine at age 9, 12, and 23 months of age without AEFI

IIV3: trivalent inactivated influenza vaccine; IIV4: quadrivalent inactivated influenza vaccine; LAIV: live attenuated influenza vaccine
Questions posed by the referring physician

- In 2013-2014 influenza season, questions for CISA
  - Should this child receive seasonal influenza vaccine?
  - Could influenza vaccine provoke SJS or worse (TEN)?
  - If CISA guidance favors vaccination, is there a preferred influenza vaccine formulation for this child?
    - LAIV
    - IIV3
    - IIV4

SJS: Stevens-Johnson syndrome; TEN: toxic epidermal necrolysis
LAIV: live attenuated influenza vaccine; IIV3: trivalent inactivated influenza vaccine; IIV4: quadrivalent inactivated influenza vaccine
Stevens-Johnson Syndrome (SJS)

- Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN): a severe skin reaction most often triggered by particular medications and some infections*
- SJS and TEN considered part of a continuum
- SJS: less severe
- TEN: more severe
- Severe damage to the skin and mucous membranes makes SJS/TEN a life-threatening condition

Assessment and discussion

- Review of literature of SJS after any vaccine
  - One published case report of SJS after influenza vaccine
  - Multicenter study from Italy quantified risk of SJS after medication* and vaccination, but did not identify vaccination as risk for SJS

- Review of SJS and TEN reports in VAERS
  - Very few reports in persons aged <18 yrs after influenza vaccine

- Discussion of risks vs. benefits of vaccination
  - Vaccinate to prevent wild-type infection (maximize protection against circulating influenza B strains)
  - Inactivated vaccine preferred over live, attenuated vaccine to eliminate possibility of vaccine strain virus replication

*Intravenous immune globulin, non-steroidal anti-inflammatory drugs
CISA guidance and follow-up

- **CISA guidance**
  - Vaccinate child with IIV4
  - Encourage all family members to be vaccinated against influenza

- **Follow-up**
  - Child received IIV4 and experienced no AEFI
  - During subsequent influenza seasons, child received LAIV and experienced no AEFI

IIV4: quadrivalent inactivated influenza vaccine; LAIV: live attenuated influenza vaccine
Sudden-Onset Sensorineural Hearing Loss after Immunization: A Case-Centered Analysis

Roger Baxter, MD¹, Ned Lewis, MPH¹, Pamela Bohrer, MD², Theresa Harrington, MD³, Laurie Aukes, RN¹, and Nicola P. Klein, MD, PhD¹

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. Case reports of sudden sensorineural hearing loss (SSHL) following vaccines have led to concerns that vaccines may rarely cause hearing loss. Because of this concern, we analyzed for an association between SSHL and vaccinations.

Study Design. We used a case-centered method, equivalent to a case control design using immunization dates from all matched members of the population to calculate exposure to vaccines, rather than sampling.


Background

Sudden sensorineural hearing loss (SSHL) is generally idiopathic but in some cases may be associated with infections, vasculitides, tumors, certain genetic conditions, and cardiovascular risk factors.¹,² Anecdotal case reports of SSHL following vaccines have speculated that vaccines might be the cause of hearing loss in some cases.³,⁷

Case Report

A healthy man in his 30s presented with sudden onset of right-sided tinnitus and hearing loss 6 days after receiving a
Sudden-onset sensorineural hearing loss (SSNHL) after trivalent inactivated influenza vaccine (IIV3)

- Healthy male in his 30s had onset of right ear fullness, tinnitus, pain, intermittent dizziness, and decreased hearing 6 days after receiving seasonal IIV3
  - No history of infection, trauma, tumor, or exposure to loud noise
  - No history of AEFI to previous vaccines
- Patient sought evaluation by primary care physician
  - Diagnosis: tinnitus
  - Initial treatment: decongestant
Sudden-onset sensorineural hearing loss (SSNHL) after trivalent inactivated influenza vaccine (IIV3)

- Right ear symptoms persisted
- Referral to ENT specialist
  - Audiogram: moderate-to-severe high frequency SSNHL of R ear
    - Audiology evaluation 6 yrs earlier was normal
  - Treatment: prednisone
    - Repeat audiogram after prednisone: severe SSNHL R ear persists
- MRI of brain: normal structure
Questions for CISA

- Did influenza vaccine cause or contribute to SSNHL?
- Guidance for future influenza vaccines?
SSNHL case discussion

- **Idiopathic SSNHL (sudden deafness)**
  - Unexplained, unilateral SSNHL occurring within <72 hours*
  - Estimated incidence: 5-20/100,000 persons annually

- **Most frequently possible causes**
  - Viral infection
  - Compromise of blood flow to labyrinth
  - Immune-mediated inner ear disease

- **Review of published literature**
  - FDA vaccine package insert: SSNHL not reported
  - One published case report of SSHNL after H1N1 infection, one after H1N1 vaccine

- **Review of vaccine components**
  - Trace gentamycin ≤ 0.15 mcg (not ototoxic level)

---

SSNHL: Sudden sensorineural hearing loss
*Idiopathic sudden sensorineural hearing loss. Rausch SD, NEJM 2008;359;833-40
SSNHL case discussion and causality assessment*

- VAERS results
  - Few case reports of SSNHL in persons <40 years for over 25-yr period
- Case-centered analysis
  - > 9 million influenza vaccines administered over 7-yr period
  - After controlling for seasonality and utilization, no increase in SSNHL following influenza or other vaccines
- Causality assessment: indeterminate (next slides)

*Halsey NA et al. Algorithm to Assess Causality after Individual Adverse Events Following Immunizations. Vaccine. 2012 Apr 13
Assessment of causality: SSNHL
Causality algorithm (cont.)
CISA guidance and patient follow-up

- **Guidance**
  - Give annual seasonal influenza vaccine

- **Follow-up**
  - Patient chose not to receive annual seasonal influenza vaccine the following influenza season
Summary

- CISA Project clinical consultation service provides a unique, free service to US-licensed healthcare providers that have complex vaccine safety questions about their patients.
- CISA Project complements other vaccine safety surveillance and consultation services at CDC’s Immunization Safety Office.
- Breadth and depth of CISA vaccine and clinical expertise and thorough case review process on 114 complex clinical vaccine safety cases have allowed CISA to provide vaccine safety actionable guidance to inform healthcare providers’ decisions for patients of all ages.
Acknowledgments

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**NCIRD**
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Candice Robinson
Rafael Harpaz
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Sherif Zaki
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**NCHHSTP**
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**NCBDPP**
Naomi Tepper

NCIRD: National Center for Immunization and Respiratory Diseases; NCEZID: National Center for Emerging and Zoonotic Infectious Diseases; NCHHSTP: National Center for HIV/AIDS, Hepatitis, STD and TB Prevention; NCBDDD: National Center for Birth Defects and Developmental Disabilities
CISA clinical case consults
Additional publication

  - Illustrates the complexity of assessing AEFI causality, and the importance of careful and complete evaluations when determining the most likely cause of an AEFI
VAERS safety signal

- Different definitions for a “signal” in the pharmacovigilance field
- The Council for International Organizations of Medical Sciences (CIOMS) proposed a signal as
  - “Information...from one or multiple sources ..., which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events...”

Results of 430 vaccine safety inquiries received by ISO, March 2017-February 2018

<table>
<thead>
<tr>
<th>What vaccines are asked about the most?</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>All vaccines or all childhood vaccine (in general)</td>
<td>119</td>
<td>28</td>
</tr>
<tr>
<td>Influenza</td>
<td>110</td>
<td>26</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>49</td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Who sends inquiries to ISO?</th>
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<tbody>
<tr>
<td>Healthcare providers (public, private or military)</td>
<td>178</td>
<td>41</td>
</tr>
<tr>
<td>General public</td>
<td>144</td>
<td>33</td>
</tr>
<tr>
<td>Public health officials (state and local health dept. staff)</td>
<td>49</td>
<td>11</td>
</tr>
</tbody>
</table>
Results of 430 vaccine safety inquiries received by ISO March 2017-February 2018 (cont.)

<table>
<thead>
<tr>
<th>What vaccines are the most frequent reasons for inquiries?</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine safety related data or information</td>
<td>263</td>
<td>61</td>
</tr>
<tr>
<td>VAERS data</td>
<td>66</td>
<td>15</td>
</tr>
<tr>
<td>Clinical advice</td>
<td>51</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>What subjects are asked about the most?</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic adverse events*</td>
<td>83</td>
<td>19</td>
</tr>
<tr>
<td>Vaccine administration issues/errors</td>
<td>49</td>
<td>11</td>
</tr>
<tr>
<td>VAERS procedures¥</td>
<td>45</td>
<td>10</td>
</tr>
<tr>
<td>Injection site reactions, shoulder injury, limb swelling, etc.</td>
<td>18</td>
<td>4</td>
</tr>
</tbody>
</table>

*Neurologic adverse events broadly defined as those affecting the brain and/or spinal cord, e.g., GBS, Bell’s palsy, encephalitis, seizure, hearing loss, brachial neuritis, Alzheimer’s disease, autism

¥Include questions on VAERS public data access, data sharing, privacy policy, reporting, follow-up, analysis methods
CISA Extra Slides
Algorithm to assess causality after individual adverse events following immunizations

Neal A. Halsey, Kathryn M. Edwards, Cornelia L. Dekker, Nicola P. Klein, Roger Baxter, Philip LaRusso, Colin Marchant, Barbara Slade, Claudia Vellozzi, the Causality Working Group of the Clinical Immunization Safety Assessment network

ABSTRACT

Assessing individual reports of adverse events following immunizations (AEFI) can be challenging. Most published reviews are based on expert opinions, but the methods and logic used to arrive at these opinions are neither well described nor understood by many healthcare providers and scientists. We developed a standardized algorithm to assist in collecting and interpreting data, and to help assess causality after individual AEFI. Key questions that should be asked during the assessment of AEFI include: Is the diagnosis of the AEFI correct? Does clinical or laboratory evidence exist that supports possible causes for the AEFI other than the vaccine in the affected individual? Is there a known causal association between the AEFI and the vaccine? Is there strong evidence against a causal association? Is there a specific laboratory test implicating the vaccine in the pathogenesis? An algorithm can assist with addressing these questions in a standardized, transparent manner which can be tracked and reassessed if additional information becomes available. Examples in this document illustrate the process of using the algorithm to determine
AEFIs “consistent with causal association” (N=21)

- Injection site large local reaction or cellulitis (6)
- Systemic allergic/hypersensitivity reactions (4)
- Febrile seizure/febrile reaction (3)
- Hypotonic hyporesponsive episode (3)
- Shoulder injury resulting from vaccine administration (2)
- Immune thrombocytopenia purpura after measles-containing vaccine (2)
- Death of child with undiagnosed severe combined immunodeficiency disease after live attenuated vaccine (1)
CISA consultation database

- Research Electronic Data Capture (REDCap) database developed by Vanderbilt University
- Case database includes
  - Patient demographics
  - Adverse event(s) and diagnoses
  - Vaccine(s) received
  - Type of consultation
  - AEFI
    - Concern for possibility of AEFI based on family history or underlying medical condition
- Assessment of causality
- Provider assessment of usefulness and satisfaction with consultation
- Patient outcome after future vaccine(s)