Vaccination Errors

Advisory Committee on Immunization Practices
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Disclaimer

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of CDC.

Topics

- Background on the CDC Immunization Safety Office (ISO)
- Vaccination errors reported to the Vaccine Adverse Event Reporting System (VAERS)
- Case series reports of vaccination errors
- Summary and prevention strategies

Background on the CDC Immunization Safety Office

Immunization Safety Office (ISO)

- **Mission**
  - Assess the safety of vaccines administered to children, adolescents and adults
- **Post-licensure vaccine safety monitoring activities**
  - Rapidly identify new or rare adverse events of clinical importance
  - Monitor changes in patterns for known adverse events
  - Assess safety in special populations (e.g., pregnant women)
  - Determine patient risk factors for particular adverse events

ISO's post-licensure vaccine safety monitoring infrastructures

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

Vaccination errors[1] reported to the Vaccine Adverse event Reporting System (VAERS)

[1] Vaccination error is defined as a preventable event that might reflect incorrect use and/or potentially result in patient harm.

Vaccine Adverse Event Reporting System (VAERS)*: co-administered by CDC and FDA

Strengths

- National data; accepts reports from anyone
- Rapid signal detection
- Can detect rare adverse events (AE)
- Collects information about vaccine, characteristics of vaccinee, adverse event†
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess if vaccine caused an AE
- Pregnancy inconsistently reported

*VAERS website: http://vaers.hhs.gov

†Some reports have no adverse event

Vaccination errors reported to the Vaccine Adverse event Reporting System (VAERS)

Vaccine 33 (2015) 3171–3178

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000–2013

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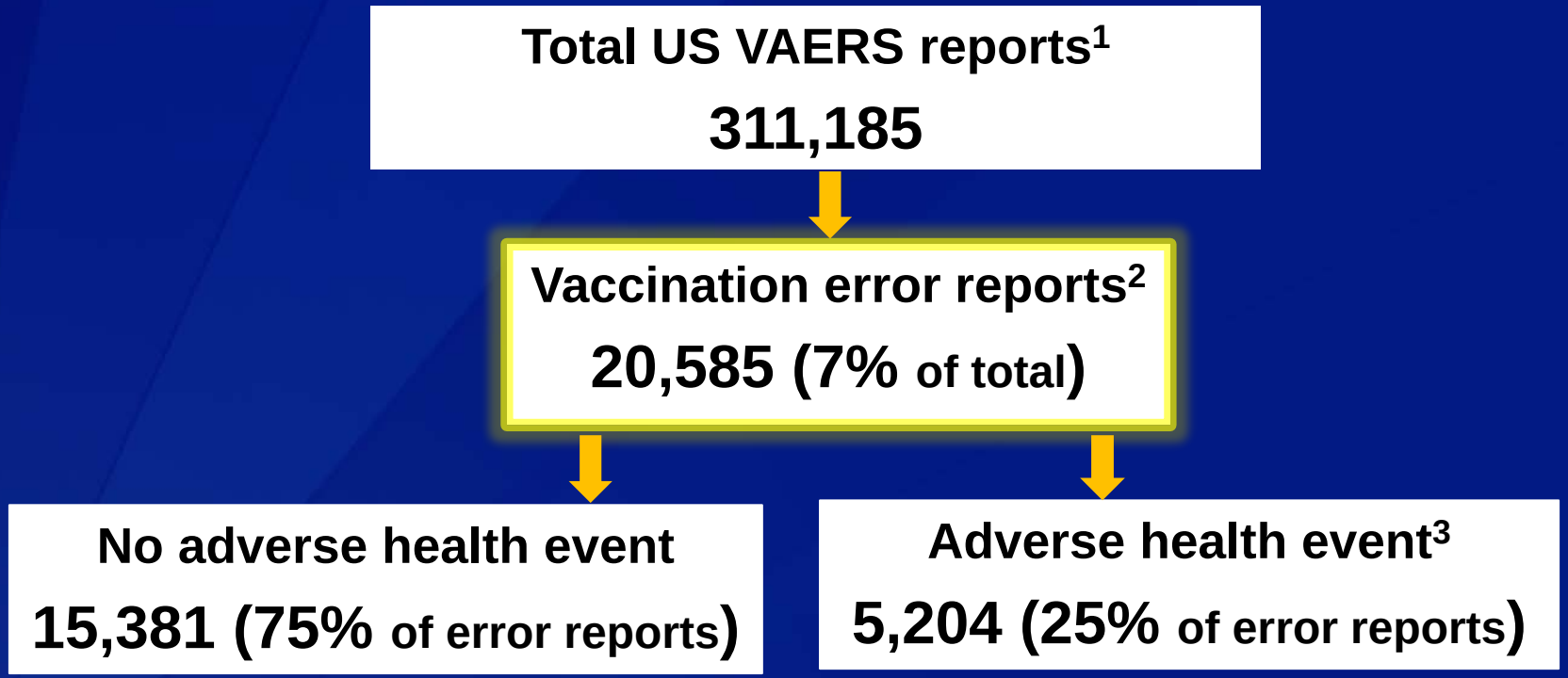
ABSTRACT

Importance: Vaccination errors are preventable events. Errors can have impacts including inadequate immunological protection, possible injury, cost, inconvenience, and reduced confidence in the healthcare delivery system.
Objectives: To describe vaccination error reports submitted to the Vaccine Adverse Event Reporting System (VAERS) and identify opportunities for prevention.
Methods: We conducted descriptive analyses using data from VAERS, the U.S. spontaneous surveillance system for adverse events following immunization. The VAERS database was searched from 2000 through

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Vaccination error reports to VAERS, 2000-2013



[1] Primary US VAERS reports
[2] Primary US VAERS reports with one or more codes describing vaccination errors
[3] Adverse health event (health problem) following vaccination

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Total reports to VAERS[1] with breakdown of error reports[2,3], 2000-2013

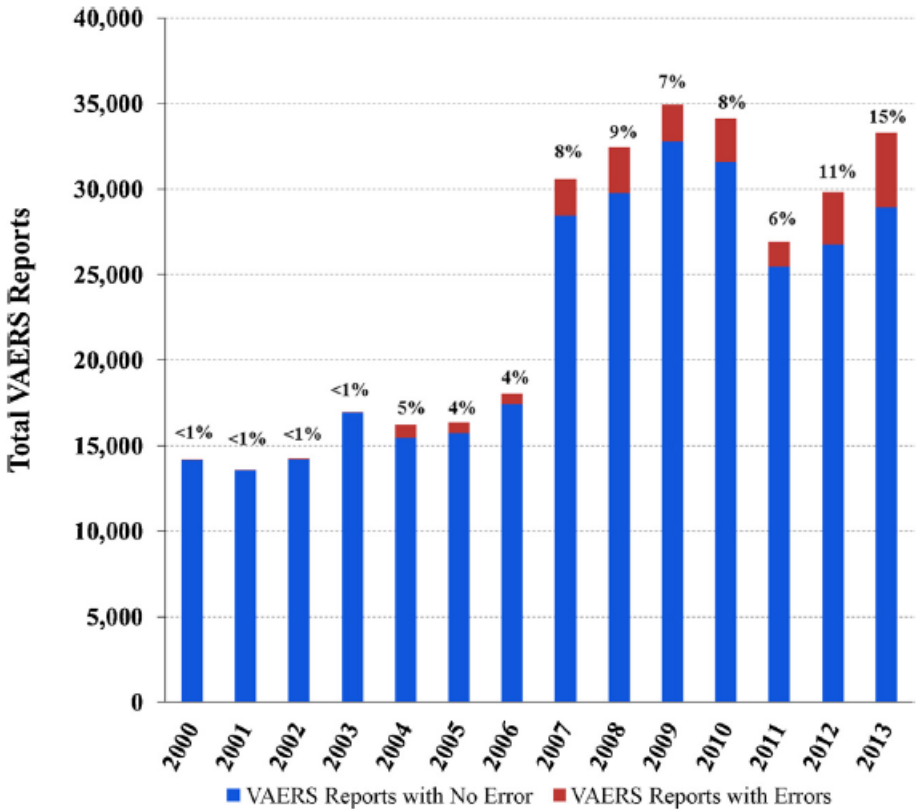


Fig. 2. *Vaccination error reports* and their percent† of all reports by year, VAERS, 2000–2013.* * 20,585 total vaccination error primary U.S. reports 2000–2013. † Percent of vaccination error reports among all primary U.S. VAERS reports by year. 311,185 total primary U.S.VAERS reports 2000–2013.

[1] 311,185 total primary US VAERS reports 2000-2013 20,585 total vaccination error reports, primary US VAERS 2000-2013; [2] 20,585 total vaccination error reports, primary US VAERS 2000-2013; [3] Percent of vaccination error reports among all primary US VAERS reports by year

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Reports by error group in VAERS, 2000-2013

~2/3 of error reports

Vaccine error group[1]	N (%)
Inappropriate schedule	5,947 (27%)
Storage and dispensing	4,983 (23%)
Wrong vaccine	3,372 (15%)
General error	2,526 (12%)
Incorrect dose	2,002 (9%)
Administration error	1,951 (9%)
Accidental exposure	373 (2%)
Product quality	239 (1%)
Contraindication	215 (1%)
Equipment	205 (1%)
Product labeling/packaging	30 (<1%)
Total errors[2]	21,843

[1] Some groupings contain more than 1 MedDRA Code; error groups are not mutually exclusive

[2] Total primary reports with errors = 20,585; an individual report may be associated with more than one vaccination error or error group depending on assigned Medical Dictionary for Regulatory Activities (MedDRA) terms (i.e., not mutually exclusive)

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Top three vaccination errors reported to VAERS, 2000-2013

1. **Inappropriate schedule errors (includes wrong age and wrong timing between doses) (5,947, 27% of total)**
   - **Children aged 0-18 years old (3,385, 57%)**
     - **53% of these errors reported in children aged <1 year old**
   - **Most common vaccines associated with wrong timing**
     - **Quadrivalent human papillomavirus vaccine (1,516)**
       - **Delays between dose 1 and dose 2[1,2]**
       - **3rd dose given too soon (12 week minimum interval)**
     - **Rotavirus vaccine (880)**
       - **First dose given after 15 weeks[1]**
       - **Last dose given after 32 weeks[1]**

[1] Based on 5% random sample review of reports wrong age inappropriate schedule (n=297),
[2] Reporter documented a delay in administration of 2nd dose (median 577 days, range 179-2067 days)

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Top three vaccination errors reported to VAERS, 2000-2013 (cont.)

2. **Storage and dispensing errors (4,983, 23% of total)**
   - **Expired vaccine administered (2,746, 55%)**
     - **Seasonal live attenuated influenza (978)**
     - **Herpes zoster (332)**
     - **Measles, mumps and rubella (218)**
   - **Incorrect storage of vaccine (2,202, 44%)**
     - **Vaccines kept outside of proper storage temperatures commonly reported (88%[1])**
       - **In 55% of these reports vaccine exposed to temperatures below recommended storage temperature**

[1] Based on 5% random sample review of reports

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Top three vaccination errors reported to VAERS, 2000-2013 (cont.)

3. **Wrong vaccine administered errors (3,372, 15% of total)**
   - **Appears to occur among vaccines with similar names, acronyms and antigens**

Common wrong vaccine mix-ups[1]		
Varicella (VARIVAX®)	with	**Herpes zoster (ZOSTAVAX®)**
Diphtheria, tetanus and pertussis (DTaP)	with	**Tetanus, diphtheria and pertussis (Tdap)**
One type of trivalent inactivated influenza vaccine (IIV3)	with	**Another type of IIV3 with a different age indication**
Pneumococcal conjugate	with	**Pneumococcal polysaccharide**
Hepatitis A	with	**Hepatitis B**

[1] Vaccine mix ups can be either combination (e.g. varicella vaccine instead of herpes zoster vaccine or herpes zoster vaccine instead of varicella vaccine)

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Adverse health events reported in 25% (5,204 of 20,585) of error reports to VAERS, 2000-2013

- Non-serious 92%, serious[1] 8%,
  - Similar percentages to non-error reports to VAERS
- Most common adverse health events
  - Injection site erythema (13%), injection site pain (11%), pyrexia (11%)
    - Similar to what's observed in non-error reports
- "Administration errors" error group had the highest percentage of reports with a documented adverse health event
  - 1,176 of 1,951 (60%) reports
  - Includes wrong site, wrong technique, incorrect route

[1]Based on the Code of Federal Regulations a report is classified as serious if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization or permanent disability

Reports of error clusters[1] to VAERS, 2000-2013

(same error, multiple individuals, same location/clinic)

- 936 error clusters involving at least 6,141 patients
  - Cluster size ranged from 2 to 501 patients (median 5)
  - 110 clusters involved 10 or more patients
  - In 586 clusters, the specific number of patients affected was stated as “unknown” or “several”
- Storage errors were the most common type of error cluster (678, 72% of all cluster reports)
  - Incorrect storage (582 clusters, 1,715 patients)
  - Expired vaccine administered (96 clusters, 1,340 patients)
    - Live attenuated influenza vaccine (45 clusters, 990 patients)

[1] Error clusters can also include events not necessarily related to vaccine itself that can have consequences that are unrelated to vaccine adverse events or effectiveness (e.g., bloodborne pathogen exposure and patient notification).

Hibbs et al. Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013. Vaccine. 2015;33:3171-8.

Case series reports of vaccination errors

Rotavirus vaccine errors*
(reports of vaccine being injected)

Morbidity and Mortality Weekly Report

Notes from the Field

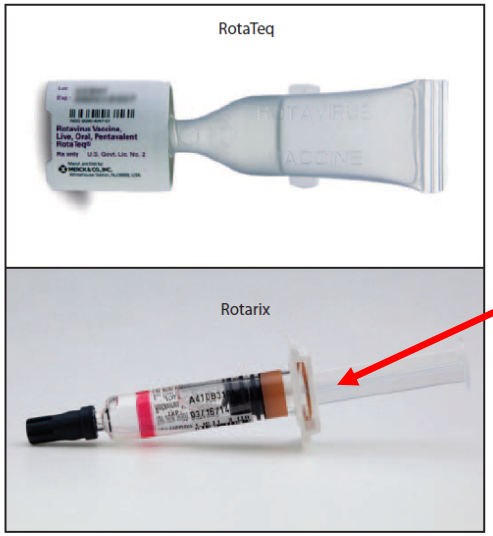
Rotavirus Vaccine Administration Errors — United States, 2006–2013

Beth F. Hibbs, MPH[1], Elaine R. Miller, MPH[1], Tom Shimabukuro, MD[1] (Author affiliations at end of text)

Two live rotavirus oral vaccines, RotaTeq (RV5) (Merck & Co., Inc.) and Rotarix (RV1) (GlaxoSmithKline Biologicals) (Figure), are approved for prevention of rotavirus gastroenteritis (*1*) and recommended at ages 2, 4 (RV5/RV1), and 6 (RV5) months by the Advisory Committee on Immunization Practices. Because most childhood vaccines are injectable, vaccination providers might have less experience administering oral vaccines. To assess that hypothesis, CDC searched for reports to the Vaccine Adverse Event Reporting System (VAERS) (*2*) of rotavirus vaccine administration errors involving injection and eye splashes in the United States during the period January 1, 2006–August 1, 2013. A total of 66 reports were found.

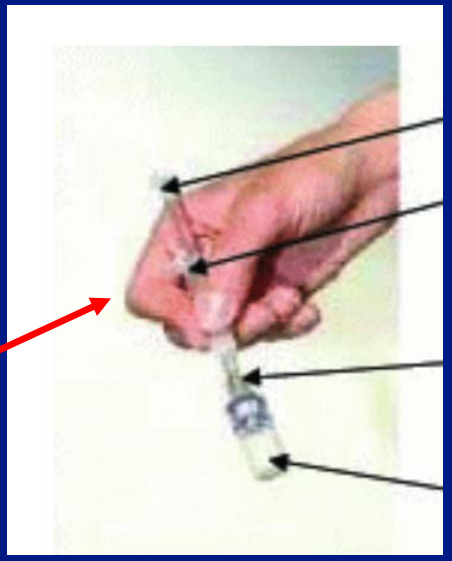
There were 39 reports of administration by injection (33 for RV1 and six for RV5). This included a cluster of six reports involving RV1 by a nurse who did not receive proper training or read the package insert. Nineteen of the 39 reports (49%) documented an adverse event; irritability (seven cases) and injection site redness (five) were the most commonly reported adverse events. Thirty of 39 reports (77%) did not have an

FIGURE. Two live rotavirus oral vaccines (RotaTeq and Rotarix)*



Photos/Merck & Co., Inc. (RotaTeq) and GlaxoSmithKline Biologicals (Rotarix)
* During the period January 1, 2006–August 1, 2013, a total of 66 reports of

FDA: Memo of Device Review (1/17/2008) - Rotarix†

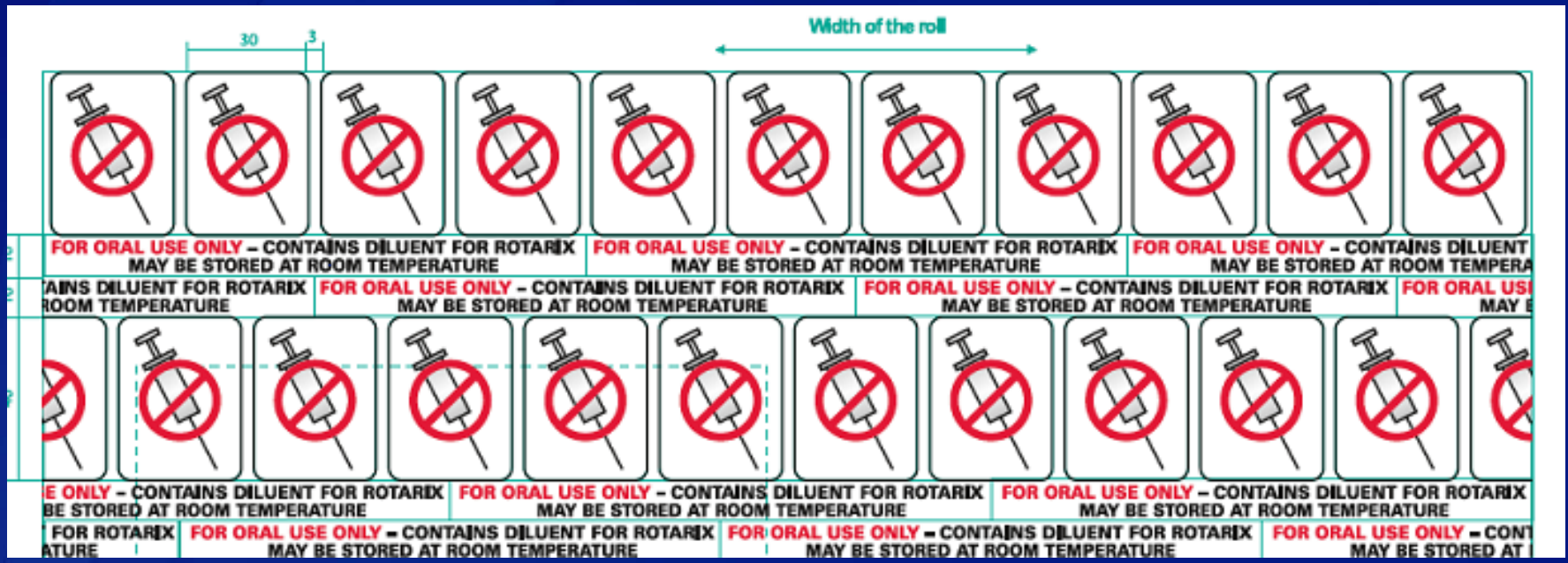


https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm133588.htm

* Hibbs et al. Notes from the field: rotavirus vaccine administration errors--United States, 2006-2013. MMWR Morb Mortal Wkly Rep. 2014;63:81.

Example of Rotarix current packaging

- The Peel-Off-Film label used in packaging the blister of the prefilled syringe diluent clearly indicates "FOR ORAL USE ONLY" in all caps, red, bold font



Graphics courtesy of GSK.

Meningococcal conjugate vaccination errors

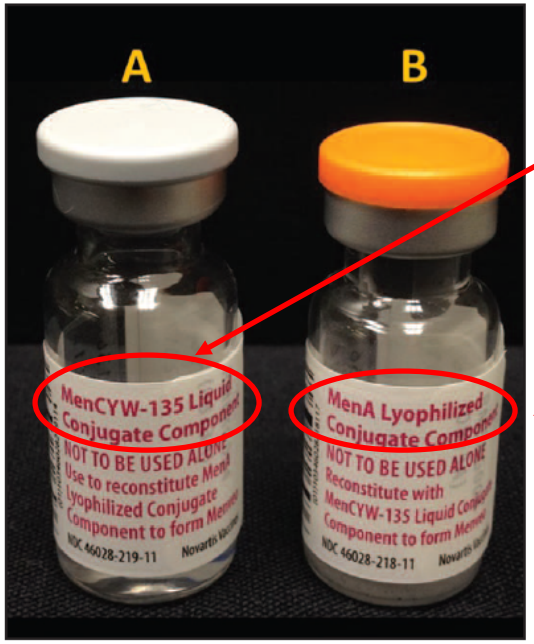
Notes from the Field

Administration Error Involving a Meningococcal Conjugate Vaccine — United States, March 1, 2010–September 22, 2015

John R. Su, MD[1]; Elaine R. Miller, MPH[1]; Jonathan Duffy, MD[1]; Bethany M. Baer, MD[2]; Maria V. Cano, MD[1]

Menveo (GlaxoSmithKline, previously Novartis AG) is a conjugate vaccine that was recommended in October 2010 for routine use in adolescents (preferably aged 11 or 12 years, with a booster at 16 years), and among persons aged 2 through 54 years with certain immunosuppressive conditions, to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135 (*1*). These recommendations have since been updated (*2*). Menveo is supplied in two vials that must be combined before administration. The MenA lyophilized (freeze-dried) component must be reconstituted with the MenCYW-135 liquid component (Figure). To administer the vaccine, the liquid component is drawn into a syringe, and used to reconstitute the lyophilized component. The resulting solution is administered by intramuscular injection. Failure to prepare Menveo as directed by the manufacturer's instructions can lead to lack of protection against the intended pathogens (*N. meningitidis* serogroups A, C, Y, and/or W-135) (*3*). Recently, an immunization provider administered only the lyophilized component of Menveo, subsequently administered a properly prepared dose of Menveo to the same patient, and asked CDC if this practice was safe. This question prompted CDC to search the Vaccine Adverse

FIGURE. Labels for the two components of Menveo conjugate meningococcal vaccine, liquid MenCYW-135 (A) and lyophilized MenA (B), both indicating that neither component is to be used alone



MenCYW-135 liquid conjugate component

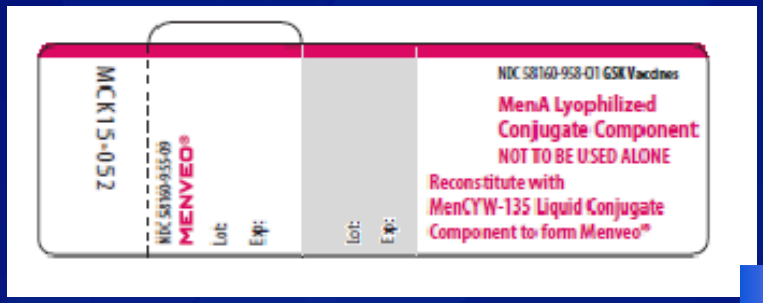
MenA lyophilized conjugate component

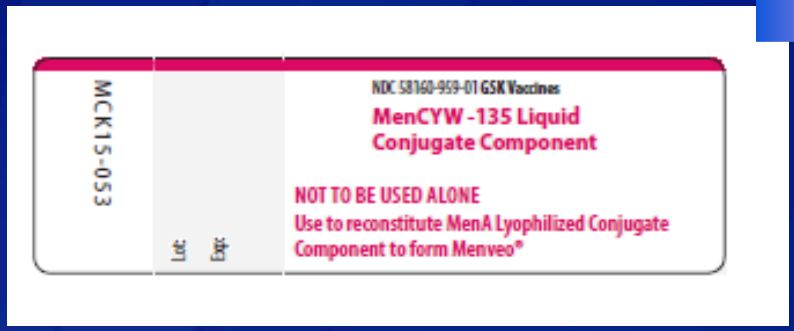
- **Menveo is supplied in two vials that must be combined before administration (liquid component used to reconstitute lyophilized component)**
- **Administration errors involved only one component of Menveo being given to patients**

Su et al. Notes from the Field: Administration Error Involving a Meningococcal Conjugate Vaccine — United States, March 1, 2010-September 22, 2015. MMWR Morb Mortal Wkly Rep. 2016;65:161-162.

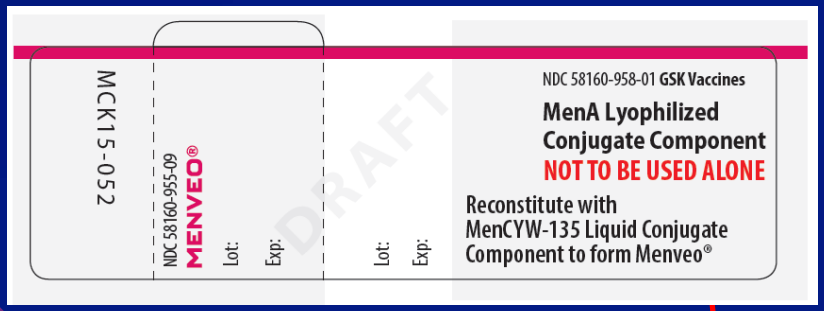
Changes to Menveo packaging after publication of “Notes from the Field” MMWR

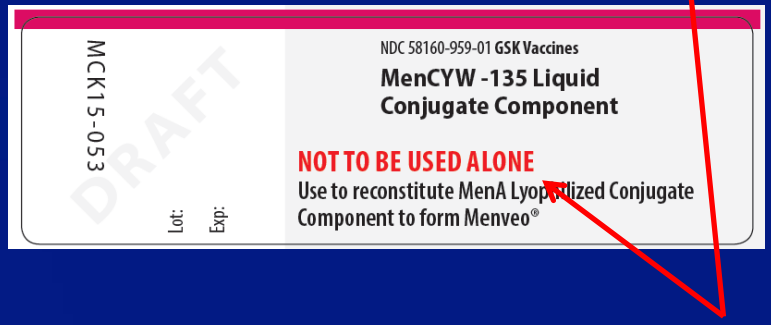
Old label





New label





Graphics courtesy of GSK.

Warning text font size increased; label font color changed to highlight warning sentence

Unintentional administration of insulin instead of influenza vaccine

Drugs Ther Perspect
DOI 10.1007/s40267-016-0333-2

SHORT COMMUNICATION

Unintentional administration of insulin instead of influenza vaccine: a case study and review of reports to US vaccine and drug safety monitoring systems

Jocelyn Clogston[1] · Lana Hudanick[2] · Tiffany A. Suragh[3] · Chris Jankosky[4] · Paige Lewis[3] · David Martin[5] · Christopher Schembri[3] · Craig Zinderman[4] · Yelena Maslov[6] · Mishale Mistry[6] · Jennifer R. Pippins[7] · Sarah Vee[6] · Jo Wyeth[6] · Tom T. Shimabukuro[3] · Jenelle Leighton[1]

Abstract

Introduction There have been isolated case reports of medication product mix-ups involving insulin unintentionally given to patients when the intent was to administer vaccines. Information on how and why these types of errors occur is limited.

Objective To describe incidents of unintentional administration of insulin instead of influenza vaccine and identify possible causes for errors.

searched Centers for Disease Control and Prevention (CDC) and US Food and Drug Administration (FDA) vaccine and drug safety monitoring databases from January 2005 to April 2015 in order to identify other incidents. We classified cases as either 'highly suggestive' or 'suggestive' of insulin and influenza vaccine mix-ups.

Results Investigation of the primary cluster incident revealed deviations from recommended practices for storage, handling, preparation, and administration of drugs and

Clogston et al. Unintentional administration of insulin instead of influenza vaccine: a case study and review of reports to US vaccine and drug safety monitoring systems. Drugs & Therapy Perspectives. 2016;32:439-446.

Summary

- Vaccination error reports comprised 6-15% of all reports to VAERS during the period 2007-2013
- The number and percentage (of total VAERS reports) of vaccination error reports have increased substantially from 2000-2013
- 75% of vaccination error reports to VAERS did not document an adverse health event
- Of the 25% of vaccination error reports to VAERS that did document an adverse health event, the adverse health events were generally similar to non-error reports

Summary (cont.)

- Based on reports to VAERS, vaccination errors usually don't appear to pose a substantial safety risk
  - However, errors do have an impact in terms of additional costs, possible effect on immunological protection, patient/ parent inconvenience, and loss of confidence in the healthcare delivery system
- Some errors do (or have the potential to) cause patient harm
  - Unintentional administration of insulin instead of vaccine (http://link.springer.com/article/10.1007/s40267-016-0333-2)
  - Reuse of syringes on multiple patients at a vaccination clinic (www.cdc.gov/mmwr/preview/mmwrhtml/mm6449a3.htm)
  - Incorrect reconstitution of measles-rubella vaccine using atracurium instead of the approved diluent (Syria) (http://www.who.int/mediacentre/news/statements/2014/interim-findings-idleb-syria/en/)

Strategies for reducing vaccination errors

- **Present**
  - Education and training on vaccine timing and spacing, especially for vaccines with complex schedules
  - Training on proper administration technique (including general injection safety)
  - Improved monitoring of vaccine storage temperatures and expiration dates
  - Improvements in differentiating vaccines and other products with similar sounding names and acronyms
  - Implementation and enforcement of procedures to properly screen for vaccine contraindications
- **Future**
  - Passive engineered interventions

Resources

- VAERS guidance on reporting vaccination errors
  https://vaers.hhs.gov/esub/index, https://vaers.hhs.gov/esub/eSubpopup.htm
- Strategies to Prevent Administration Errors (in the Pink Book)
  www.cdc.gov/vaccines/pubs/pinkbook/vac-admin.html
- CDC Vaccine Storage & Handling Tool Kit
  www.cdc.gov/vaccines/recs/storage/toolkit
- One & Only Campaign
  www.cdc.gov/injectionsafety/1anonly.html
- Technically Speaking: Vaccine Administration Errors (CHOP)
  http://www.chop.edu/news/technically-speaking-vaccine-administration-errors

CDC activities

- CDC Vaccination Error Work Group

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Craig Zinderman
Yelena Maslov
Mishale Mistry
Jennifer Pippins
Sarah Vee
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Saint Louis County Department of Public Health

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Jenelle Leighton

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Atlanta, GA

National Center for Emerging and Zoonotic Infectious Diseases

Division of Healthcare Quality Promotion – Immunization Safety Office

Thank You

For more information please contact Centers for Disease Control and Prevention
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Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

Extra slides

Groupings of vaccine error codes (11 groups)

Accidental
- Accidental exposure
- Accidental exposure to product
- Accidental needle stick

Administration errors
- Drug administered at inappropriate site
- Drug administration error
- Incorrect drug dosage form administered
- Incorrect drug administration duration
- Incorrect route of drug administration
- Multiple use of a single-use product
- Wrong technique in drug usage process

Contraindication
- Contraindication to vaccination
- Documented hypersensitivity to administered drug
- Labeled drug-drug interaction medication error

Equipment
- Injury associated with device
- Medical device complication
- Needle issue
- Syringe issue

General
- Medication error
- Vaccination error

Inappropriate schedule
- Inappropriate schedule of drug administration
- Drug administered to patient of inappropriate age

Incorrect dose
- Accidental overdose
- Drug dose omission
- Extra dose
- Incorrect dose administered
- Underdose
- Overdose
- Multiple drug overdose

Product quality
- Product contamination,
- Product contamination microbial
- Product contamination physical
- Product quality issue

Product labeling/packaging
- Drug name confusion
- Product label confusion
- Product name confusion
- Product container issue
- Product label issue
- Product label on wrong product
- Product outer packaging issue
- Product packaging issue
- Product packaging confusion

Storage and dispensing
- Drug dispensing error
- Expired drug administered
- Incorrect product storage
- Incorrect storage of drug
- Poor quality drug administered
- Product reconstitution issue

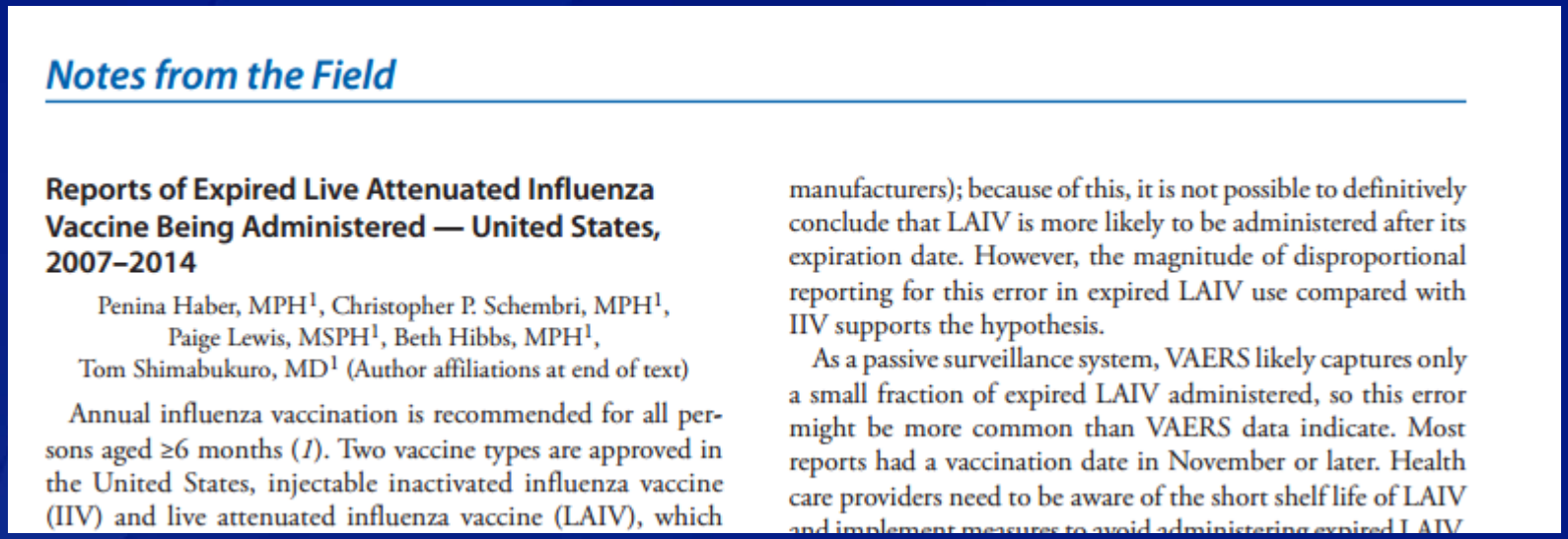
Wrong drug
- Drug dispensed to wrong patient
- Wrong drug administered

Contraindication error group (215, 1% of total)

- Drug exposure during pregnancy (120, 56%)
  - 93% involved live attenuated influenza vaccine
  - Adverse health events described in 15% of reports (18)
    - 7 adverse health events were pregnancy related:
      - Spontaneous abortion (6)
      - Vaginal bleeding (1)

- Other contraindication errors reported
  - Live vaccines given to persons with immunodeficiency conditions
  - Vaccines given to persons with a history of an allergic reaction to a vaccine component
  - Live attenuated influenza administered to persons with asthma

Reports of Expired Live Attenuated Influenza Vaccine Being Administered – United States, 2007–2014



Notes from the Field

Reports of Expired Live Attenuated Influenza Vaccine Being Administered — United States, 2007–2014

Penina Haber, MPH[1], Christopher P. Schembri, MPH[1], Paige Lewis, MSPH[1], Beth Hibbs, MPH[1], Tom Shimabukuro, MD[1] (Author affiliations at end of text)

Annual influenza vaccination is recommended for all persons aged ≥6 months (*1*). Two vaccine types are approved in the United States, injectable inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV), which

manufacturers); because of this, it is not possible to definitively conclude that LAIV is more likely to be administered after its expiration date. However, the magnitude of disproportional reporting for this error in expired LAIV use compared with IIV supports the hypothesis.

As a passive surveillance system, VAERS likely captures only a small fraction of expired LAIV administered, so this error might be more common than VAERS data indicate. Most reports had a vaccination date in November or later. Health care providers need to be aware of the short shelf life of LAIV and implement measures to avoid administering expired LAIV

Haber et al. Notes from the field: reports of expired live attenuated influenza vaccine being administered--United States, 2007-2014. MMWR Morb Mortal Wkly Rep. 2014;63(35):773.

Reporting vaccination errors to VAERS

- **Please report all significant adverse events that occur after vaccination of adults and children, even if you are not sure whether the vaccine caused the adverse event. The Vaccine Adverse Event Reporting System (VAERS) accepts all reports, including reports of vaccination errors.**
- **VAERS is primarily concerned with monitoring adverse health events and we encourage reporting of clinically significant adverse health events following vaccination. Using clinical judgment, healthcare professionals can decide whether or not to report a medical error at their own discretion.**
  - **For example, a healthcare professional may elect to report vaccination errors that do not have an associated adverse health event, especially if they think the vaccination error may pose a safety risk (e.g., administering a live vaccine to an immunocompromised patient) or that the error would be preventable with public health action or education.**

VAERS web site https://vaers.hhs.gov/index