Update on post-licensure safety monitoring of recombinant zoster vaccine (RZV, Shingrix)

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October 29, 2020

Disclaimer

- The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of CDC and FDA
- The use of product trade names is for identification purposes only

VAERS

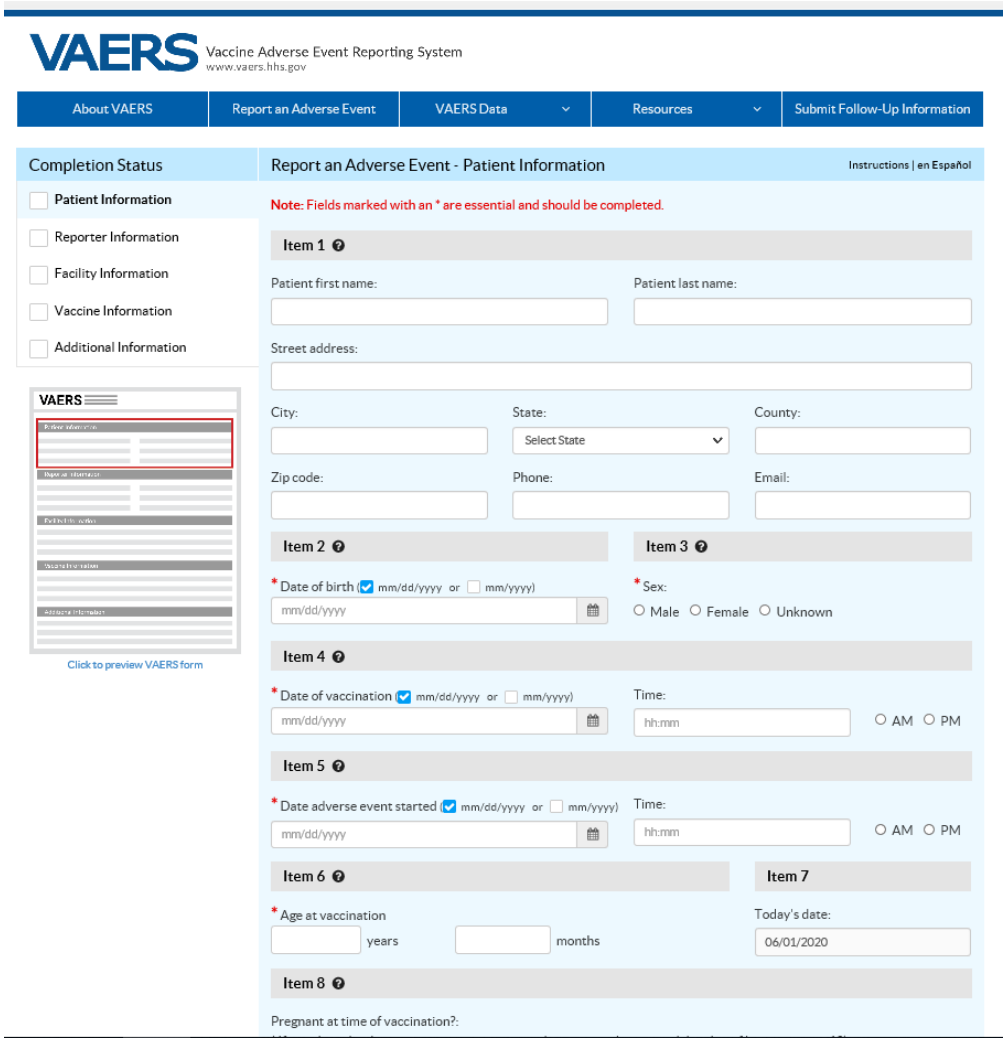
Vaccine Adverse Event Reporting System

Co-managed by CDC and FDA

http://vaers.hhs.gov

Reporting to VAERS – by website

- Fillable PDF also available



Vaccine Adverse Event Reporting System (VAERS)

- VAERS accepts *all* reports from *all* reporters
  - Doesn't judge causality or clinical severity of the event
- "Early-warning system": identifies potential vaccine safety concerns for study in more robust data systems

Strengths

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess causality

MMWR (2019) and RZV (Shingrix)

- Most reports nonserious
- Most AEs systemic or at injection site

TABLE 2. Most commonly reported symptoms* after receipt of recombinant zoster vaccine (RZV) in reports submitted to VAERS (N = 4,381)† — United States, October 2017–June 2018

Sign/Symptom	Total RZV reports, no. (%)	RZV given in combination with other vaccines, no. (%)
Pyrexia	1,034 (23.6)	57 (26.6)
Injection site pain	985 (22.5)	49 (22.9)
Injection site erythema	880 (20.1)	50 (23.4)
Pain	853 (19.5)	45 (21.0)
Chills	847 (19.3)	32 (15.0)
Headache	730 (16.7)	30 (14.0)
Fatigue	703 (16.0)	23 (10.7)
Pain in extremity	691 (15.8)	37 (17.3)
Injection site swelling	588 (13.4)	29 (13.6)
Myalgia	530 (12.1)	19 (8.9)

TABLE 1. Characteristics of recombinant zoster vaccine (RZV) reports submitted to VAERS — United States, October 2017–June 2018

Report characteristic	No. (%)
Total reports	**4,381 (100)**
Sex	
Women	2,870 (65.5)
Men	1,265 (28.9)
Not reported or unknown	246 (5.6)
Seriousness*	
Nonserious	4,251 (97.0)
Serious†	130 (3.0)
Type of reporter	
Health care professional	1,661 (37.9)
Manufacturer	1,661 (37.9)
Patient	801 (18.3)
Other	236 (5.4)
Parent/Guardian/Caretaker	22 (0.5)
Age group (yrs)	
<50§	27 (0.6)
50–59	956 (21.8)
60–69	1,467 (33.5)
70–79	988 (22.6)
≥80	251 (5.7)
Not reported or unknown	692 (15.8)
RZV given alone¶	**4,167 (95.1)**

Reports to VAERS following RZV

- Current as of Oct 22, 2020
  - No appreciable changes proportion-wise since MMWR or Apr 2019

Report characteristics	N (%)
Total reports	38,902
Female	25,723 (66.1)
Non-serious	37,885 (97.4)
Type of reporter	
Manufacturer	14,289 (36.7)
Healthcare professional	13,003 (33.4)
Patient	9,540 (24.5)
Other	2,070 (5.3)
Age groups (years)	
<50†	195 (0.5)
50-59	8,307 (21.4)
60-69	13,293 (34.2)
70-79	8,282 (21.3)
80+	2,267 (5.8)
Not reported or unknown	6,558 (16.9)
RZV given alone	36,044 (92.7)

*Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization or permanent disability (FDA routinely reviews all serious reports)

†RZV not approved for use in <50 y/o

Most common signs and symptoms reported to VAERS following RZV

Signs and symptoms (MedDRA Preferred Terms)*	38,902 total reports n (%)
Pyrexia (fever)	9,294 (23.9)
Chills	7,965 (20.5)
Pain	7,820 (20.1)
Headache	7,444 (19.1)
Injection site pain	7,359 (18.9)
Fatigue	6,362 (16.4)
Pain in extremity	6,165 (15.8)
Injection site erythema	5,609 (14.4)
Myalgia	4,424 (11.4)
Nausea	4,223 (10.9)

- No appreciable changes proportion-wise since Apr 2019
  - Most AEs systemic or at injection site
  - No unexpected adverse events or patterns of reporting detected

*Not mutually exclusive; a report may contain more than one MedDRA Preferred Term

Guillain Barre Syndrome (GBS) after Shingrix

- During Oct 2017–Apr 2019, 46 reports of GBS
  - 31 met Brighton Level 1–3 diagnostic certainty (24) or were physician-diagnosed (7)
    - BL 1 (2); BL 2 (17); BL 3 (5)
    - 29 (94%) developed symptoms within 42 days of vaccination
- During May 2019–October 2020, 44 reports of GBS
  - 27 met Brighton Level 1–3 diagnostic certainty (16) or were physician diagnosed (11)
    - BL 1 (3); BL 2 (9); BL 3 (4)
    - 25 (93%) developed symptoms within 42 days of vaccination

Data mining

- Proportionality reporting ratios (PRR) and Empirical Bayesian (EB) data mining identified no disproportional reporting of AEs after Shingrix compared to other vaccines
  - EB data mining: “Product administered to patient of inappropriate age” (ages 19-44.9 years)

Summary of VAERS review of RZV reports

- As of Oct 2020, RZV post-licensure safety monitoring findings in VAERS are generally consistent with the safety profile observed in pre-licensure clinical trials
  - Most reported AEs systemic or at injection site
  - Serious AEs rare (2.6% of reports, similar to other vaccines administered to same age groups)
  - Number, composition of reported GBS comparable to last update
- No disproportional reporting of any AEs by PRR or EB data mining
  - Inappropriate age (19–49.9 years) by EB data mining

Acknowledgements

CDC

Ruth Gallego
Penina Haber
Charles Licata
Paige Marquez
Elaine Miller
Pedro Moro
Christine Olson
Traci Roberts
Tiffany Suragh
Tom Shimabukuro
Frank Destefano

FDA

Bethany Baer
Jane Baumblatt
Manette Niu
Narayan Nair
Jane Woo
Craig Zinderman

GDIT

Kavita Kripalani
Elisa Lara
Stacey Neloms

Thank you

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