



Summary of HZ Work Group Interpretation of RZV Safety Data

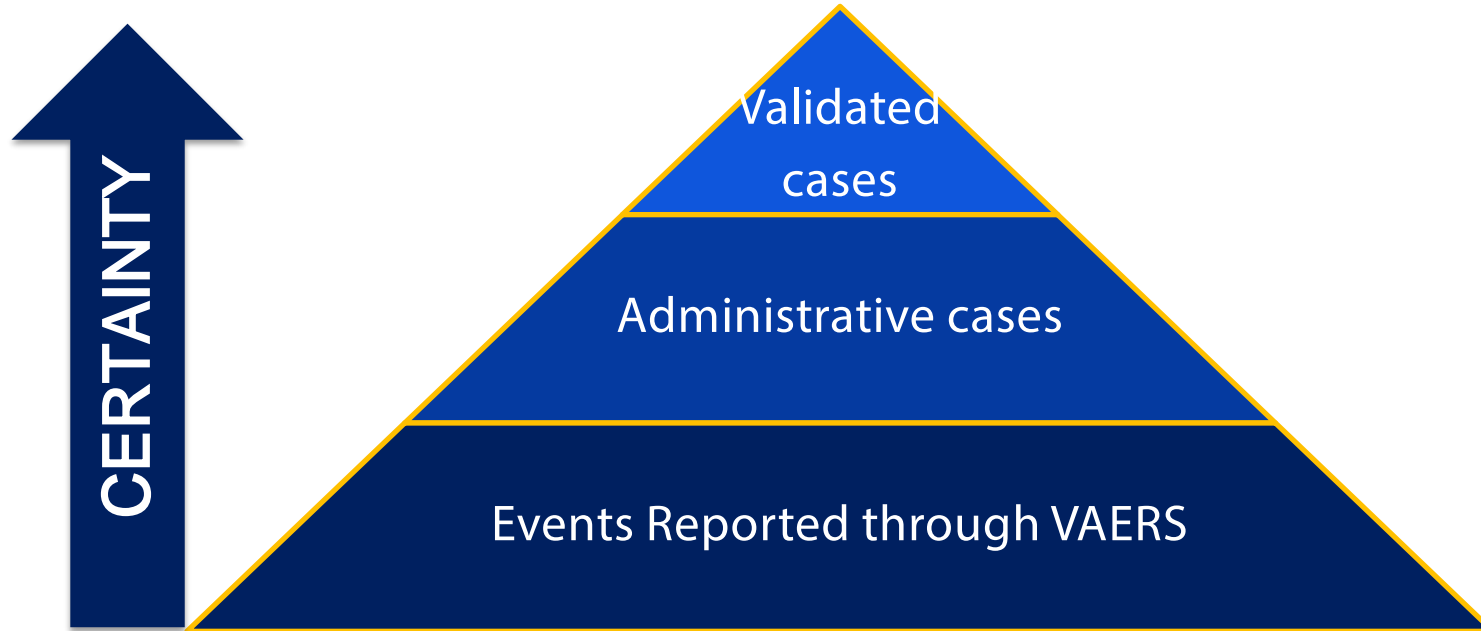
Dr. Kathleen Dooling MD MPH

HZ Work Group Liaison

ACIP June 26, 2019

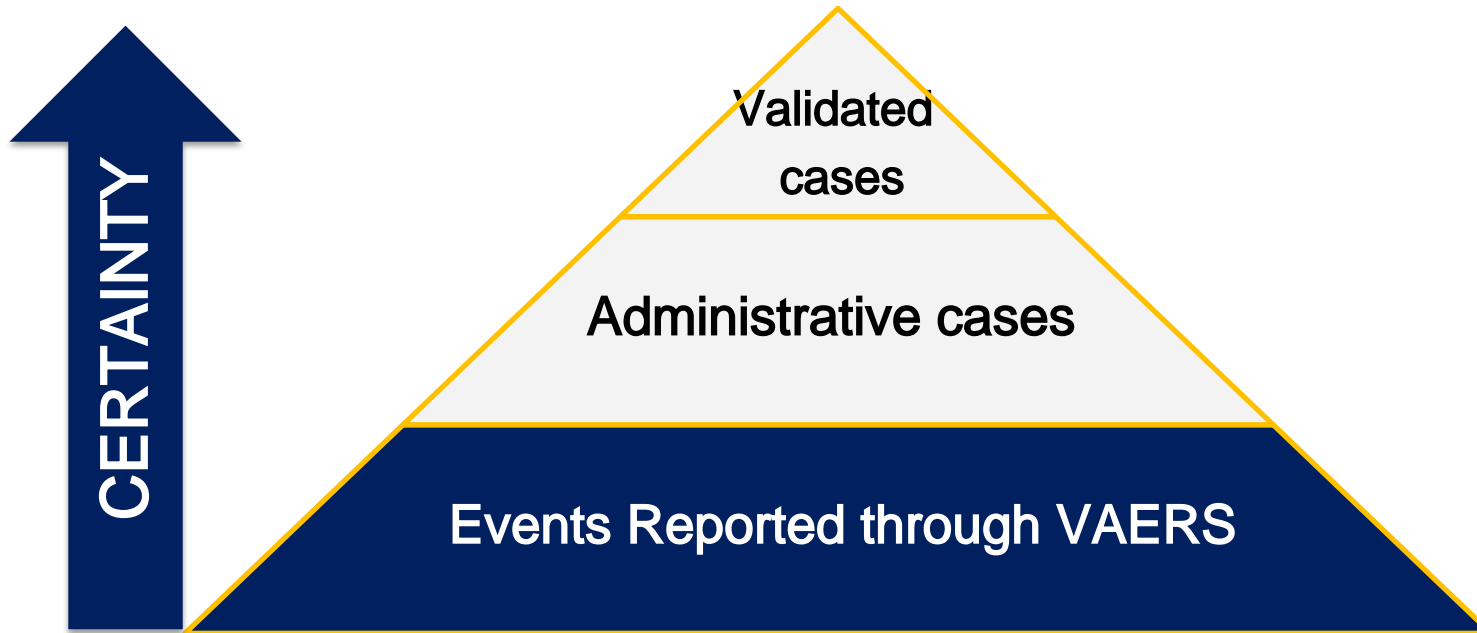
HZ Work Group Interpretation of RZV Safety Data

- ~12 M doses RZV doses distributed in the U.S.
- Reports of reactogenicity-like symptoms-- consistent with RCTs
- Preliminary statistical signals for Bell's Palsy and Guillain-Barré syndrome (GBS)



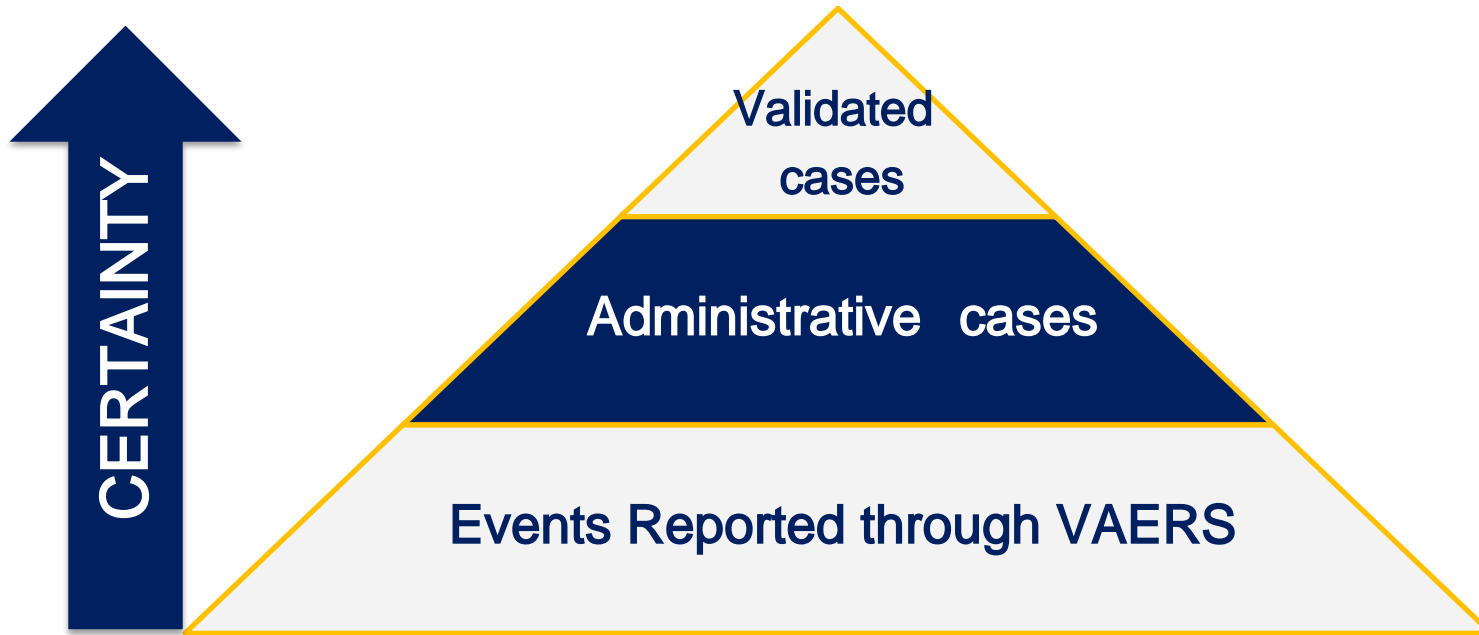
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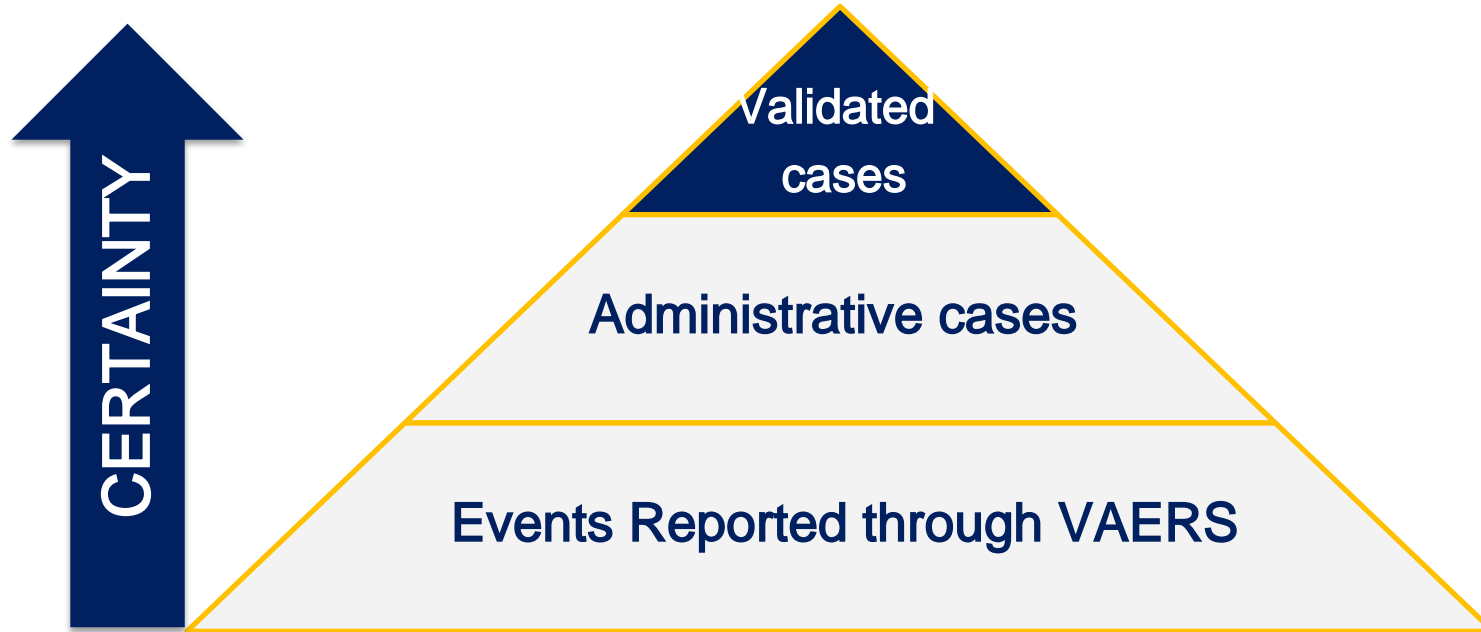
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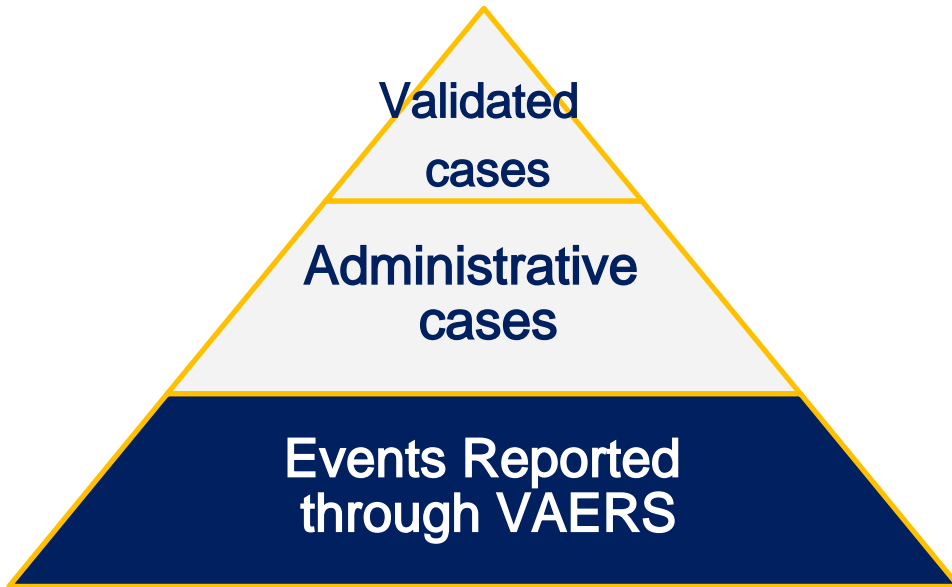


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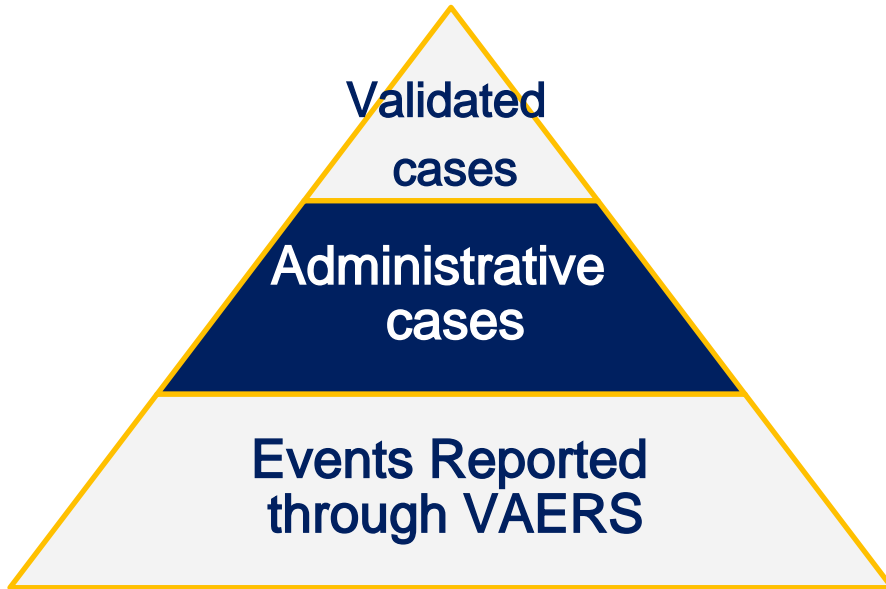


Investigation of Bell's Palsy following RZV- VAERS



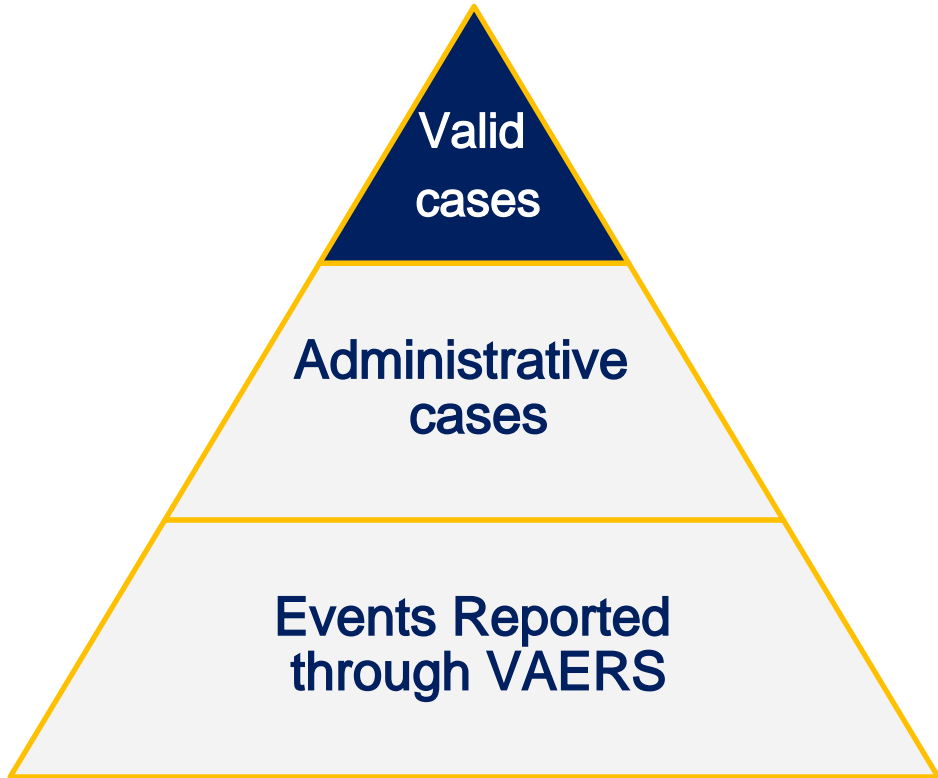
- No signal in VAERS

Investigation of Bell's Palsy following RZV- Admin cases



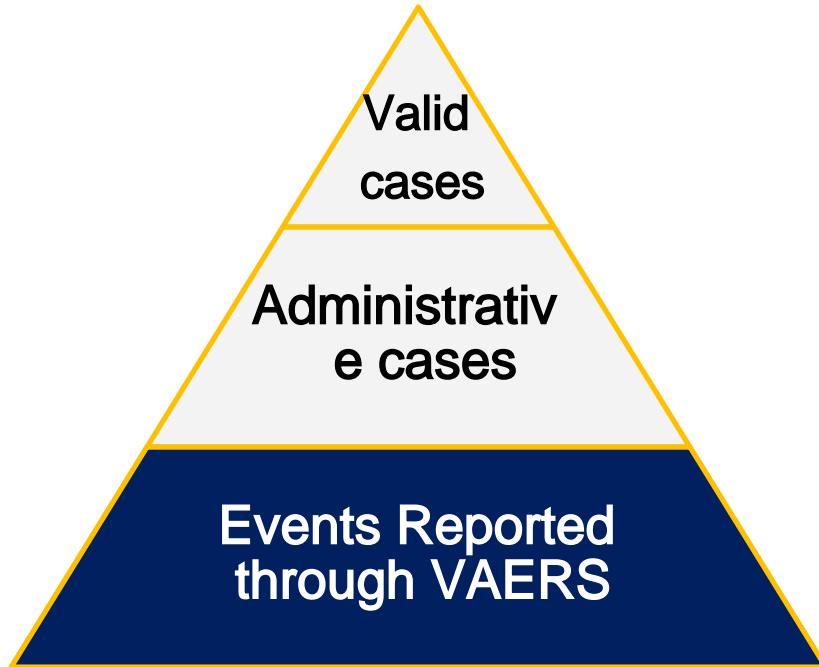
- **↑ RR in VSD**
- **No ↑ RR with other comparison groups**
- **No signal in VAERS**

Investigation of Bell's Palsy following RZV- Validated cases



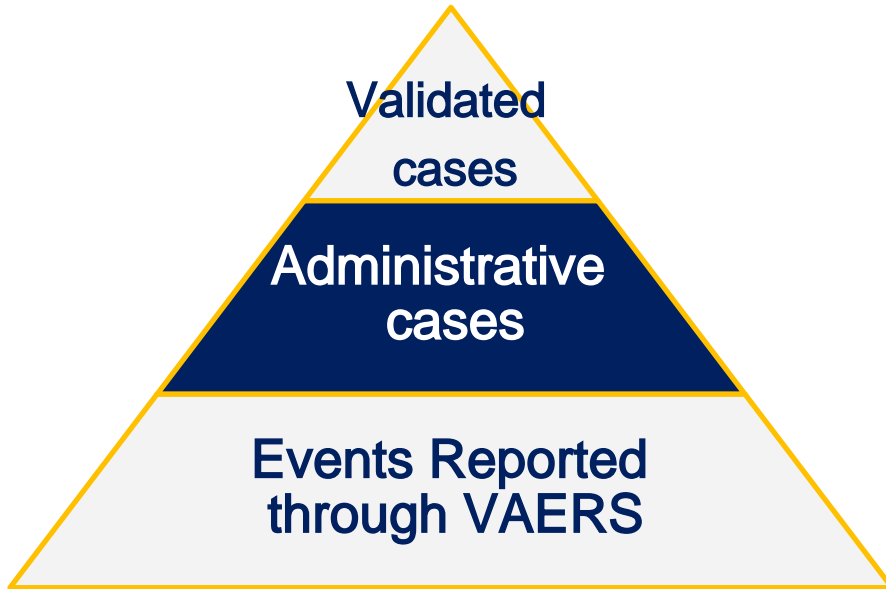
- **15 of 36 (42%) cases validated**
- RR= 1.3 in VSD
- No \uparrow RR with other comparison groups
- No signal in VAERS

Investigation of GBS following RZV- VAERS



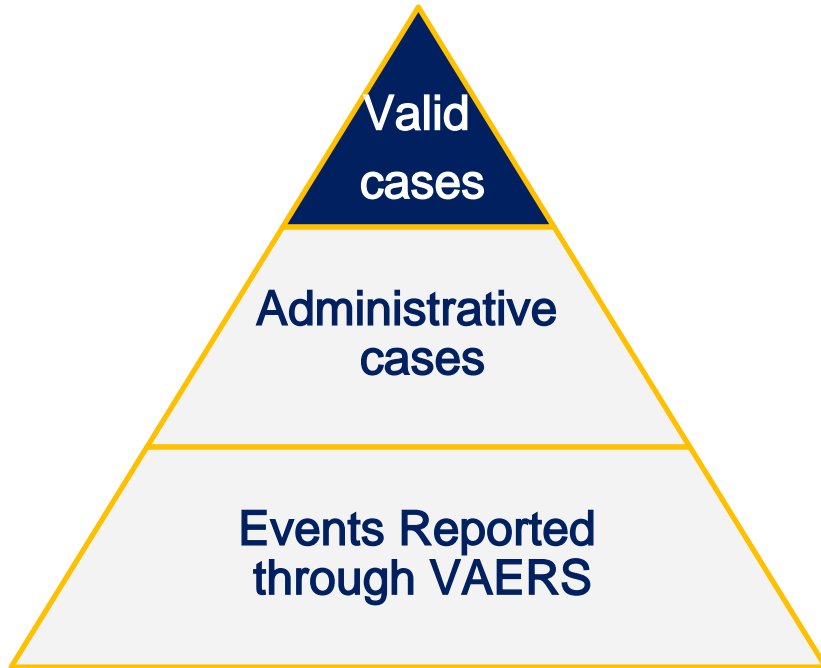
- No signal in VAERS

Investigation of GBS following RZV- Admin cases



- **↑RR in VSD & Medicare**
- **Lower RR with concurrent comparators**
- **No signal in VAERS**

Investigation of GBS following RZV- Validated cases



- Validated GBS: RZV=2, ZVL=2
- Risk difference for RZV-ZVL: 4.7-5.9 cases/100,000 py
- ↑RR, large confidence intervals
- ↑RR in VSD & Medicare
- Lower RR with concur compar.
- No signal in VAERS

Summary of HZ Work Group Discussions

- **GBS is rare and interpretation of elevated risk of GBS is uncertain given only 2 validated cases in RZV and ZVL groups**
- **Due to wide confidence intervals that overlap baseline rates, current data are insufficient to determine if a safety problem exists**
- **HZ Work Group members agree that there is insufficient evidence at this time to support a change in policy or practice**
- **HZ Work Group agrees with the proposed next steps:**
 - **Continue enhanced monitoring and clinical case review of Bell's Palsy and GBS reports following RZV in VAERS**
 - **Continue to track and chart validate cases of Bell's Palsy and GBS in VSD**
 - **Chart validate GBS cases in Medicare and pursue self-controlled analytic options**

Questions

Outcome #4: Serious adverse events

Estimates of effect (ZOE-50 and ZOE-70)

Outcome	No. of subjects (# studies)	No. reported in controls (%)	No. reported in vaccinated (%)	Difference
Serious adverse event*	29,311 (1)	1,900 (13.0%)	1,842 (12.6%)	0.4%
Serious adverse events considered related to vaccine**	29,311 (1)	15 (0.1%)	15 (0.1%)	0.0%

- The remaining 7 studies administered HZv to a total of 616 participants and found no serious adverse events related to vaccination

*Throughout study period (mean follow up = 4.6)

**ZOE50: The three serious adverse events (SAE) considered to be related to vaccination by the investigators in the HZv were immune thrombocytopenic purpura, musculoskeletal chest pain, and nervous system disorder.

**ZOE70: the SAEs considered by the investigator to be related to the trial intervention in the HZv were lymphadenitis, acute myocardial infarction, ulcerative colitis, acute pancreatitis, administration site erythema, administration site pain, chills, pyrexia, allergic granulomatous angiitis, bacterial arthritis, erysipelas, herpes zoster, eczema, neutropenic sepsis, and acute myeloid leukemia. Some participants had more than one event. One death in the HZv group was considered by the local investigator to be related to the vaccination.

Outcome #5: Reactogenicity (Grade 3 rxn[§])

Estimates of effect (ZOE-50 and ZOE-70)

Outcome	No. of subjects (# studies)	No. reported in controls (%)	No. reported in vaccinated (%)	Difference
Any Grade 3 reaction*	9,936 (1)	155 (3.1%)	820 (16.5%)	13.4%
Grade 3 injection- site reaction**	9769 (1)	17 (0.3%)	460 (9.4%)	9.1%
Grade 3 systemic reaction**	9762 (1)	116 (2.4%)	528 (10.8%)	8.4%

§"Grade 3 injection site = redness and swelling at injection site >100 mm or preventing normal activity
Grade 3 systemic = temperature (oral) >39°C or preventing normal activity

*Solicited and unsolicited report of a Grade 3 reaction within 7 days after vaccination

** Solicited report of Grade 3 reaction within 7 days after vaccination