

NVAC H1N1 Vaccine Safety Risk Assessment Working Group (VSRAWG) Update

National Vaccine Advisory Committee
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Charge

To conduct independent, rapid reviews of available federal immunization safety monitoring data for the 2009 H1N1 influenza vaccines

Working Group Members

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Progress

- Regularly reviewed H1N1 safety data
 - Initial meeting November 2, 2009
 - 14 meetings to-date
 - Awaiting end-of-season analyses for final report
- Reports to NVAC
 - Dates
 - December 16, 2009
 - January 20, 2010
 - February 26
 - March 23
 - April 23
 - June 2
 - Transmitted to the ASH -> ASPR, CDC, FDA, NIH, IHS, CMS, DoD, VA & International Partners
 - Available on NVPO website at:
<http://www.hhs.gov/nvpo/nvac/reports/index.html>

VSRAWG Report

Influenza Vaccine Distribution

Since May 3, 2010 (data cut-off used in the last formal report):

- A total of 127,040,020 doses have been distributed (105,284,820 inactivated and 21,755,200 live, attenuated).

Summary of Reports to date

- Guillain-Barré Syndrome: EIP data detected a weak signal, other systems have not crossed that threshold. The estimated attributable risk is 1 excess case per 1 million persons vaccinated
- Bell's Palsy: Two systems detected a weak signal. In one system, several analyses to examine this finding yielded inconsistent results with only the one comparisons providing support for the signal while others did not
- Thrombocytopenia / Idiopathic Thrombocytopenic Purpura: Three systems detected a weak signal. Medical records are being reviewed to see if the diagnostic codes are valid.

What to consider when assessing the strength of a signal

- strength of the association (e.g. elevated relative risk in a controlled study)
- temporal relationship between the receipt of the product and onset of the event
- consistency of findings across available data
- evidence of a dose response effect
- potential biologic mechanisms linking the vaccine and the adverse event
- the rigor of the methodology and analyses being employed

Interpreting a weak signal

- Since many analyses in several systems are being conducted simultaneously, there is a good possibility that temporal associations will arise by chance alone
- A “weak signal” implies a low level of risk and/or substantial methodological limitations in data or study design
- Before any assessment of the association of vaccine exposure and adverse event is possible, several steps are needed to assure the validity of the findings and to explore potential alternatives that might result in a spurious association

Steps in Signal Evaluation – 1

1. Check data quality
2. Check whether comparison groups are defined appropriately
3. Conduct the analysis using a different control group (e.g., concurrent vs. historical) or different vaccine

Steps in Signal Evaluation– 2

4. Conduct a temporal scan to see if outcomes cluster during a post-vaccination time window
5. Conduct a definitive study using logistic regression analysis
6. Review charts to confirm or exclude cases as true cases

Experience in VSD

- Monitored 5 vaccines and 30 vaccine-outcome pairs
- 21 generated no signal
- 9 signals were investigated internally and found spurious
- 1 signal was investigated with much input and was widely reported (MMRV and seizures)

Reasons for False Signals

- Miscoding of outcomes in ICD9s (2)
- Misaligned comparison data (3)
 - Temporal trends
 - Confounding by age
 - Mismatched outcome definitions
- Imprecise background rates for rare outcomes (1)
- Chance – especially for rare events that occur early (3)

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- End-of-season analyses, which are in progress, will be important for determining whether the signals outlined in this report are spurious or if they represent a true association
- The Working Group does not view these results as necessitating any immediate response by NVAC, but wishes that the NVAC be aware of progress to date

Moving Forward

- Working Group will review end on end-of-season analyses
- Expect majority of analyses to be complete by mid-October 2010
- Future VSRAWG meetings:
 - September 27
 - October 25
 - November 22
- Final VSRAWG report to NVAC in February 2011