

Monitoring the Safety of a Novel Influenza Vaccine

Melinda Wharton, MD, MPH

**Captain, US Public Health Service
Acting Director, Immunization Safety Office
Centers for Disease Control and Prevention
Atlanta, GA**



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Planning for Vaccine Safety Monitoring

- No decisions made yet about full production and use of a vaccine for novel H1N1 influenza
- If we do recommend use of a novel influenza vaccine, vaccine safety monitoring will be an important aspect of the program
- Planning now so we can be prepared to implement safety monitoring if vaccination is undertaken

Planning Challenges

- **Concurrent use with seasonal influenza vaccines**
- **Multiple manufacturers**
- **Possibility of adjuvanted vaccine**
- **Anticipated need for 2 doses in at least some persons**
- **Possibility of unanticipated adverse events**
- **Vaccination of a large number of people in a short time**
- **Historical experience with A/New Jersey/1976 vaccine**

More Planning Challenges

- **Lack of certainty about**
 - target groups for initial use of vaccine
 - In which settings vaccine will be administered

Guillain-Barré Syndrome

- An acute inflammatory demyelinating polyneuropathy of unknown origin, thought to be of autoimmune origin
- May be triggered by antecedent infection
 - *Campylobacter jejuni*
 - Respiratory infections
- Incidence rate in adults about 2 per 100,000 person-years
 - increases with increasing age

Guillain-Barré Syndrome and the A/New Jersey/1976 Vaccine

- National Influenza Immunization Program suspended December 1976, when preliminary data suggested an increased risk of GBS among vaccinees
- Subsequent analyses suggested an attributable risk of vaccine-related GBS among adults of about 1 case per 100,000 vaccinees

Guillain-Barré Syndrome and Other Influenza Vaccines

- **Studies of subsequent influenza vaccines have not found a consistent association with GBS, and when it has been found, the attributable risk has been small**
 - **U.S. 1992-1993 and 1993-1994 seasons combined: about one case per 1,000,000 persons vaccinated**

Objectives for Safety Monitoring

- **Timely identification of clinically significant adverse events following receipt of novel influenza vaccine**
- **Rapid assessment of significance of adverse events**
- **Evaluation of the risk of GBS associated with the novel influenza vaccine**

Timely Identification of Clinically Significant Adverse Events

- **Enhanced surveillance through the Vaccine Adverse Event Reporting System**
- **Active surveillance using sequential analytic methods through one or more Vaccine Safety Datalink sites**

Enhanced Surveillance through VAERS

- **VAERS is**
 - National in scope
 - Flexible
 - Scalable
 - Designed to accept reports from vaccinees
- **Enhancements**
 - Comprehensive communications efforts to support reporting, including providing information at the time of vaccination
 - Facilitate reporting of manufacturer and lot number by providing written record

Active Surveillance using Sequential Analytic Methods

- **Allows rapid assessment of prespecified adverse events**
 - Simultaneous analysis with appropriate comparison group
 - Chart confirmation is feasible
- **Can relatively quickly identify events that are of highest priority for further investigation**
- **Will require that accurate information on vaccination be available in managed care databases**

Rapid Assessment of Significance of Adverse Events

- **Certain pre-specified adverse events can be assessed through sequential analytic approach**
- **Approaches for other adverse events:**
 - **Rapid study utilizing linked immunization and outcome records**
 - **Comparison of observed cases with expected cases, based on known incidence rates**
 - **Field investigation, in collaboration with State Health Departments**

Evaluation of the Risk of GBS Associated with the Novel Influenza Vaccine

- **Active, unbiased case finding of incident GBS cases in multiple areas**
- **Ascertainment of vaccination status and other risk factors for GBS**
- **Will be seeking expert input into planning**

Unresolved Issues

- **Role of Vaccine Safety Datalink sites in vaccine administration under state and county plans**
- **How to facilitate collection of accurate information on manufacturer and lot number**