

National Vaccine Advisory Committee

2009 H1N1 Influenza Update

NIAID/NIH Clinical Trials

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Outline

- **NIAID H1N1 vaccine studies**
- **Status update**
- **Clinical infrastructure**
 - **acknowledgements**

H1N1 Outbreak: Initial Response

- **FDA, NIAID, HHS initiated regular discussions on vaccine development, study design**
- **FDA - licensure discussions with companies**
- **CDC, other labs developed reference viruses**
- **BARDA - US H1N1 vaccine supply/industry**
 - **possible large scale immunization program**
 - **clinical trial material**
- **NIAID - identify options for USG clinical trial support**

Areas identified for NIAID trial support

■ Help inform policy, “gap” areas

- rapid availability of 1 vs. 2 dose data in different populations
- administration with seasonal influenza vaccine
- different dosing intervals
- use of different adjuvanted products
- mixing vaccines and adjuvant from different companies

■ Special populations

- young infants, pregnant women, immunocompromised

NIAID H1N1 Vaccine Trials: Initial Studies

- 5 separate protocols
- Data not intended to support licensure; obtain rapid assessment of safety, immune responses
 - 1-week post dose blood samples, subset of cohort
- 1 vs. 2 dose studies
 - CSL vaccine; healthy adults/elderly (18 years +)
 - SP vaccine; healthy adults/elderly (18 years +)
 - SP vaccine; healthy children (6 mo to 17 years)
- Co- vs. sequential administration TIV + H1N1
 - SP vaccine; healthy adults/elderly (18 years +)
 - SP vaccines; children (6 mo to 17 years)

NIAID H1N1 Studies: 1 vs. 2 Dose Study in Healthy Populations

- **Goal: rapid availability of immunogenicity data**
 - 2 doses: 15µg or 30µg, ~ 21 days apart
 - adult trials; 2 protocols SP, CSL vaccines (n = 400 each)
 - 100 (18-64y), 100 (65y+); per dose group
 - pediatric trial; SP vaccine (n = 600)
 - children (6mo to < 36mo, 3y to 9y, 10y to 17y)
 - 100 per dose group in each age stratum
 - endpoints: safety and immunogenicity
 - 6 month safety follow up
 - 4-fold rises, proportion with titer \geq 1:40 by HAI at day 21, 42
 - Immunogenicity points: pre and 21 days post each dose
 - early blood draws: 8 to 10 days post vaccinations
 - subset of vaccinated subjects
 - **Lead PIs: Pat Winokur (CSL), Univ. Iowa; Karen Kotloff, UMD (SP)**

Early Results: 1 vs. 2 doses studies

- **ongoing safety assessment**
 - **local and systemic reactions**
 - vaccines are safe and well tolerated – adult, elderly, pediatric populations
 - no serious adverse events associated with vaccination
- **CSL: NEJM article by Greenberg et. al. Sept. 10, 2009**
 - at 21 days, a single 15ug dose of the CSL H1N1 vaccine was immunogenic
- **NIAID release of early time point data; September 11, 2009**
 - **healthy adults, elderly**
 - **subset of age/dose strata**
 - **results 8 to 10 days post first dose**
 - **% HAI response \geq 1:40 (similar results by microneut assay)**
 - **18 – 64 years of age**
 - Sanofi 15ug dose: 96% (18 to 64 years), 56% (65 years+)
 - CSL 15ug dose: 80% (18 to 64 years), 60% (65 years+)

H1N1 Vaccine Studies: Co- and Sequential Administration

- **Goal: Assess impact on vaccination responses**
 - H1N1 vaccine before, after, or at the same time as TIV
 - 2 doses, 15 µg sanofi pasteur H1N1 vaccine, 21 days apart
 - 1 dose TIV

- 400 adults (18-64y), 400 elderly (65y+); enrolled
- 600 children (50 per group); enrolling
 - 6mo to < 36mo, 3y to 9y, 10y to 17y

- endpoints: safety and immunogenicity
 - safety follow up: 6 months post dose 2
 - 4-fold rises, proportion with titer \geq 1:40 by HAI
- **Lead PI: Sharon Frey, St. Louis Univ.**

Mixing Vaccines and Adjuvant

- **HHS pandemic preparedness vaccine strategy**
- **Assess safety and immunogenicity mixing stockpiled vaccine antigens and adjuvants from different manufacturers**
 - vaccines: CSL and sanofi pasteur H1N1 vaccines
 - adjuvant: GSK's AS03
 - mixed prior to administration
 - protocol: 3.75 μ g +AS03, 7.5 μ g and 15 μ g +/- AS03
 - 2 doses, 21 days apart
 - status: screening for sanofi pasteur/AS03 study started; CSL/AS03 IND in preparation
 - **Lead PIs: Lisa Jackson, Seattle Group Health (SP); Kathryn Edwards; Vanderbilt (CSL)**

NIAID H1N1 Vaccine Studies: Pregnant women

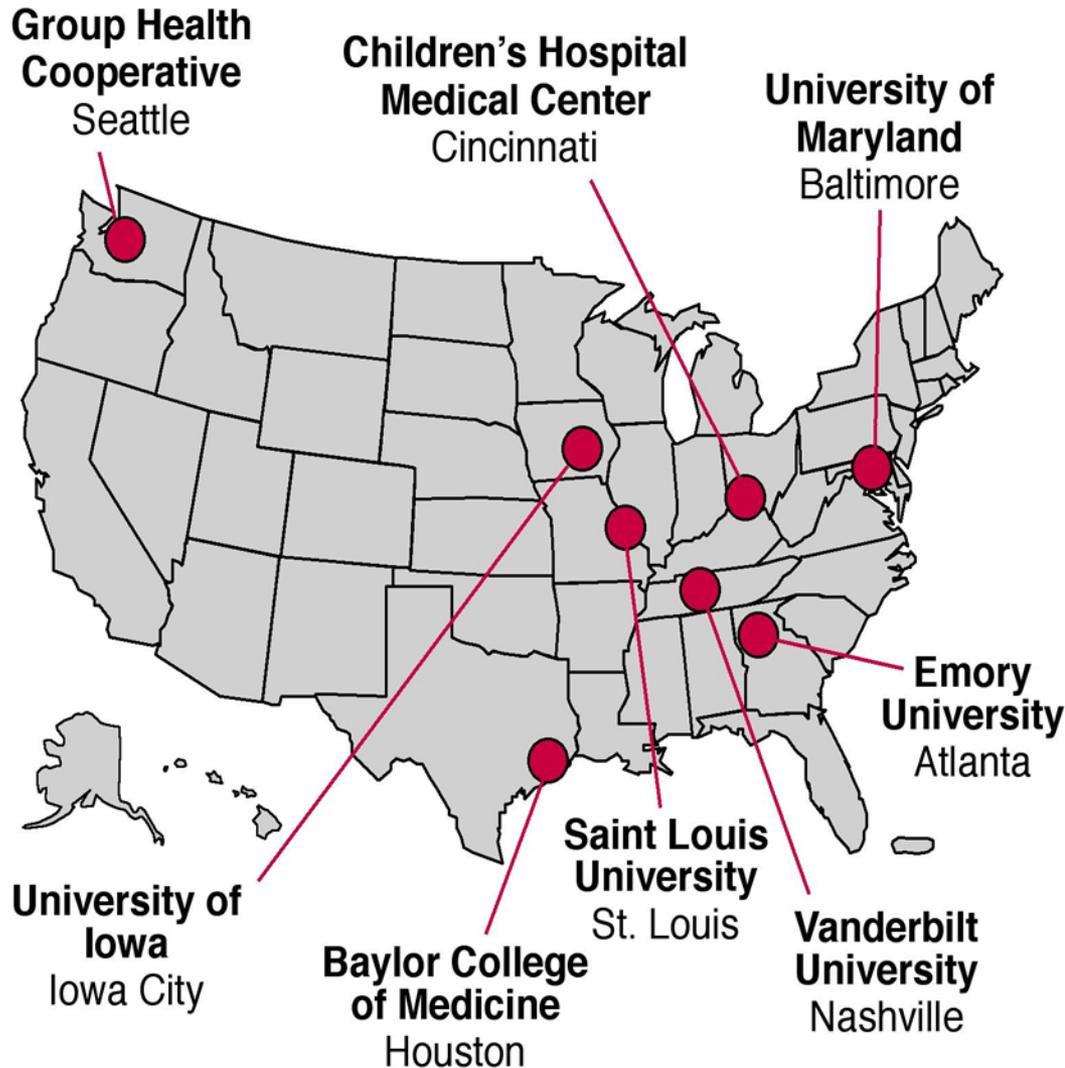
■ **3 studies planned**

- Sanofi – started September 9, 2009
- Novartis – planned
- CSL – planned
- 2 doses of the vaccine: 15 μ g or 30 μ g, ~ 21 days apart
- 120 women, 18 to 39 years of age
- Second or third trimester
- endpoints: safety and immunogenicity
 - Safety follow up: 6 months post dose 2
 - 4-fold rises, proportion with titers \geq 1:40 by HAI
- **Lead PI: Lisa Jackson, Group Health (SP)**

ACKNOWLEDGEMENTS I

- **DHHS, BARDA contracts provided all H1N1 vaccine**
- **FDA, CDC**
- **Industry colleagues**
- **VTEU investigators, coordinators, volunteers**
 - **Baylor College of Medicine**
 - **Cincinnati Children's Hospital**
 - **Emory University**
 - **University of Iowa**
 - **University of Maryland**
 - **Seattle Group Health Cooperative**
 - **St. Louis University**
 - **Vanderbilt University**
 - **Subcontract sites**
 - **Duke University, Durham**
 - **Univ Texas Medical Branch at Galveston**
 - **Children's Mercy Hospital, St. Louis**
 - **Scott and White Memorial Hospital, Temple Texas**
 - **Stanford University**

NIH's Network of Vaccine and Treatment Evaluation Units (VTEUs)



- Established in 1962
- >160 Phase I, II, and III clinical trials since 1995
- Trials of
 - Seasonal vaccines
 - Pre-pandemic vaccines
 - Antivirals
- \$189M over 7 years, avg \approx 27M/yr (FY08-FY14)

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ACKNOWLEDGEMENTS cont'd

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- **SRI Birmingham**
- **Fisher Bioservices**
- **PPD**
- **Safety Monitoring Committee Members**
- **NIAID colleagues**