

# National Vaccine Advisory Committee

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2009 H1N1 Influenza Update

NIAID/NIH Clinical Trials

**September 16, 2009**

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# Outline

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

# H1N1 Outbreak: Initial Response

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- **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

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## ■ 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

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- **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

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- **Goal: rapid availability of immunogenicity data**
  - 2 doses: 15 $\mu$ g or 30 $\mu$ g, ~ 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

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- **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

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- **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

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- **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 $\mu$ g +AS03, 7.5 $\mu$ g and 15 $\mu$ 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

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## ■ 3 studies planned

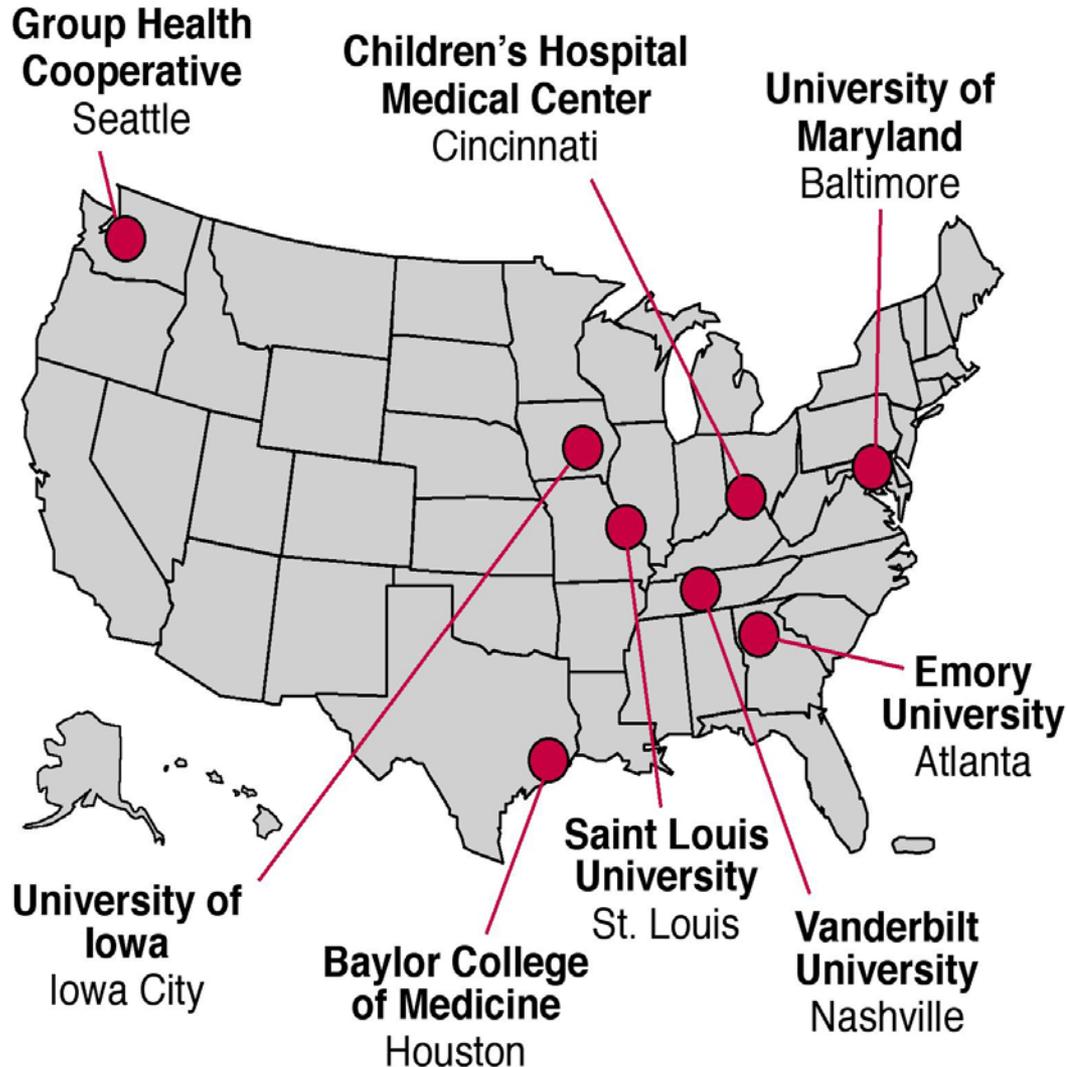
- Sanofi – started September 9, 2009
- Novartis – planned
- CSL – planned
- 2 doses of the vaccine: 15 $\mu$ g or 30 $\mu$ g, ~ 21 days apart
- 120 women, 18 to 39 years of age
- Second or third trimester
- endpoints: safety and immunogenicity
  - Safety follow up: 6 months post dose 2
  - 4-fold rises,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

# ACKNOWLEDGEMENTS I

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