H1N1 Pandemic: HHS Perspective - Vaccines

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HHS/ASPR/BARDA
U.S. 2009-H1N1 Vaccine Strategy

VACCINE DEVELOPMENT
- Clinical Sample Isolation
- Virus Reference Strain Prep.
- NDV/Influenza Variants Prep.
- Clinical Interim Clinical Issues
- Clinical Studies Antigen and Adjuvant

EPIDEMIOLOGY OF THE VIRUS
- Determination of virus severity and transmissibility in populations

PCAST
- NVAC
- NBSB
- VRBPAC
- ACIP

VACCINE MANUFACTURING
- Potency Assay Reagents Prep. and Calibration
- Commercial Scale Bulk Antigen Manufacturing Without Adjuvant
- Commercial Scale Bulk Antigen Manufacturing With Adjuvant
- Bulk Adjuvant Manufacturing
- Seasonal Flu Southern Hemisphere 2009
- Vaccine Formulation Fill-Finish
- Commercial Scale Syringes/Needles

H1N1 1st Wave
- Seasonal Flu Vaccine Bulk Antigen Mfg. – NH
- Seasonal Flu Vaccine Formulation Fill Finish Manufacturing – NH
- Seasonal Flu Vaccine Manufacturing – SH

H1N1 2nd Wave
- Monitoring Effectiveness & Safety
- Vaccine Distribution & Administration
- Immunization Planning

Mar 09
Apr 09
May 09
Jun 09
Jul 09
Aug 09
Sept 09
Oct 09
Nov 09
Dec 09
Jan 10
Feb 10
H1N1 Vaccine Products
Standard vaccine – U.S.-licensed

- Multi-dose vial
- Single-dose Syringe
- Intranasal Sprayer

- CSL
- Novartis
- sanofi pastuer
- GSK
- MedImmune

- Inactivated, subunit vaccine
- Live, attenuated vaccine
# U.S. H1N1 Vaccine Manufacturing – Distribution

<table>
<thead>
<tr>
<th>Vaccine Manufacturers</th>
<th>Central Distributor</th>
<th>States &amp; Locals Sites</th>
<th>American Public</th>
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<tbody>
<tr>
<td>5 sanofi pasteur</td>
<td>4 distrb. sites</td>
<td>~150,000</td>
<td>Up to 300 million</td>
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<td>Novartis</td>
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<td>GlaxoSmithKline</td>
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<tr>
<td>Ancillary Product Suppliers</td>
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- **Vaccine Manufacturers**
  - sanofi pasteur
  - Novartis
  - GlaxoSmithKline
  - MedImmune
  - CSL

- **Central Distributor**
  - McKesson

- **States & Locals Sites**
  - State Health Depts
  - County Public Health Depts
  - Other Public Sites
    - School clinics
    - Private Providers
  - Ancillary Product Suppliers

- **American Public**
  - Children
  - Healthcare Workers
  - Children Caregivers
  - Pregnant Women
  - Underlying Chronic Disease
  - General Public

**Ancillary Product Suppliers**

- BARDA
- CDC
- STATES
- LOCALS
H1N1 Vaccine Lessons Learned

• **Vaccine Development**
  – HHS experience with manufacturers & VTEUs paid off well

• **Vaccine Manufacturing**
  – Better methods needed to select & archive high growth virus strains
  – Better production methods needed for manufacturing seasonal & pandemic vaccine
  – More domestic bulk vaccine manufacturing capacity needed
  – Clear communication of vaccine capacity vs. actual vaccine production when potency assay data needed to set more reasonable expectations on vaccine availability
  – More rapid and better vaccine potency assay needed
  – Fill finish manufacturing into multidose vials for inactivated vaccine
  – Sharing of working virus seed stocks and manufacturing information among manufacturers
  – Sooner rehearsals of new production lines
  – Utilization of veterinary flu vaccine manufacturing expertise on swine flu strains
More Lessons Learned from H1N1 Pandemic

• Having a commercial market changes the game
• Dual usage principle exemplified by influenza vaccines
• Vaccine development, manufacturing, & distribution, & administration are vital links in the pandemic vaccine program
• HHS interagency collaboration was key to success
• Collaboration/transparency with industry is just as important
• Find ways to reduce undue influence in science and decision-making
• Crises can bring out the best in everyone involved
• Expect the unexpected
• Don’t forget the role of the public
Future Directions

• **Short term**
  – Countermeasure Enterprise Review ordered by Sec. Sebelius
  – Complete, expand, & expedite pandemic influenza countermeasure development & manufacturing infrastructure building following after action reviews
  – Potency assays: SRID assay → new methods (e.g., mass spec) reduce from 8-12 weeks → days
  – Sterility assays: std. 14 day → 5 day assay
  – Virus seed selection for high growth & library of possible pandemic strains
  – Expanded domestic fill finish manufacturing network

• **Mid-term**
  – Cell-based vaccines with clinical virus isolates passaged in cells to make virus reference strains (1-2 weeks savings)

• **Long term**
  – Recombinant- and molecular-based vaccines that are non-dependent on virus growth (up to 8 weeks savings)