Vaccines

Operationalization of Pandemic Plans – from Plan to Action

Influenza A (H1N1): Lessons Learned and Preparedness

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Topics to be covered

- Types of vaccines potentially available
- Critical Scientific Questions to be Answered
- Global Needs
- Possible Vaccine Supply
- Logistics
- Need for Equity
- Financing
Potentially Available Vaccines

- Split Virus – manufactured in eggs similarly to present seasonal vaccines
- Split Virus – manufactured in cells
- Whole Virus, inactivated
- Live attenuated vaccines
- Products not yet licensed
  - Viral-like particles (VLPs)
  - Recombinant
- Stretching the vaccine supply
  - Adjuvants
    - Oil-in Water
    - Other
Scientific Questions to Be Resolved Which Will Impact Vaccine Supply I

- What are the target populations for vaccination?
  - Critical Infrastructure – health care, other
  - Traditional groups at high risk of complications for influenza
  - Children and/or young adults
  - General population or sub-groups within the general population
- How many doses will be needed?
- How much antigen will be needed per dose?
- Will adjuvanted vaccine be acceptable?
Examples if the potential impact of an oil in water adjuvant on immunogenicity of H5N1 split virus Influenza vaccine

### Percentage $\geq 32$ HI titer $^+$

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>1.9 mcg adjuvant</th>
<th>3.8 mcg adjuvant</th>
<th>7.5 mcg adjuvant</th>
<th>15 mcg adjuvant</th>
<th>7.5 mcg adjuvant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24</td>
<td>29</td>
<td>40</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>Dose 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>81</td>
<td>89</td>
<td>86</td>
<td>34</td>
</tr>
<tr>
<td>% cross reacting antibody</td>
<td>4</td>
<td>9</td>
<td>17</td>
<td>23</td>
<td>0</td>
</tr>
</tbody>
</table>

Scientific Questions to Be Resolved Which Will Impact Vaccine Supply II

- What will be the yields using current reference H1N1 strains?
- What will be the virulence of the next wave?
- What are the goals of a vaccination program?
  - Prevention of deaths and severe disease?
  - Prevention of morbidity and economic disruption
  - Maintaining critical infrastructure
- Will seasonal vaccine at normal quantities still be needed?
Projected Global Impact of Severe a Pandemic

An estimated 96% of deaths during a severe influenza pandemic will occur in developing world

Murray CJ et al. Lancet 2006;368:2211-18
Developing country doses will depend on the countries and populations targeted.

Country Population Segmentation, Non-Self Producing (millions)

<table>
<thead>
<tr>
<th>Income Level</th>
<th>Total Population (M)</th>
<th>% of Total Population Represented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0%</td>
</tr>
<tr>
<td>Low Income</td>
<td>1,654</td>
<td>625</td>
</tr>
<tr>
<td>Lower Middle Income</td>
<td>631</td>
<td>270</td>
</tr>
<tr>
<td>Upper Middle Income</td>
<td>377</td>
<td>165</td>
</tr>
<tr>
<td>Total</td>
<td>2,662</td>
<td>1,060</td>
</tr>
</tbody>
</table>

Source: UNPD population dataset
Source: Oliver Wyman, 2008
Coverage requirement
Depending upon the definition of essential populations, 0.4 – 3% of low and middle-income countries’ populations would required coverage with H1N1 vaccine.

H1N1 vaccine “essential populations” strategies
(Includes 153 low and middle-income countries without current access to H1N1 vaccine)

- **Minimum Care**: 0.4% - 1% - 2%
- **Security and Stability**: 1.2% - 2.2% - 3.0%
- **Social Infrastructure**: 2.2%
- **Security and Infrastructure**: 3.0%

**Populations Covered by Strategy (Based on Country Feedback)**
- **Minimum Care**: Health care workers
- **Security and Stability**: Health care workers, Key gov. personnel, Emergency workers, Military
- **Social Infrastructure**: Health care workers, Key gov personnel, Essential services (utilities, transport, communications)
- **Security and Infrastructure**: Health care workers, Key gov. personnel, Emergency workers, Military, Essential services

Source: Oliver Wyman, 2008
Pandemic vaccine baseline capacity was estimated at 94.5M doses per week

Assumptions / Methodology

- Survey sent to 36 potential influenza vaccine manufacturers
  - 100% response rate
  - All 21 current influenza vaccine producers responded
  - 26 manufacturers that intend to produce pandemic vaccines
  - Includes LAIV and one recombinant vaccine capacity

- Survey assumes
  - 1:1 H1N1 to seasonal yields
  - Most dose sparing formulation for each manufacturer
  - Use of full production capacity

Estimated H1N1 Vaccine Capacity
At 1:1 yields, most dose-sparing formulation, full capacity

Source: Marie-Paule Kieny, WHO, presentation titled “Assessment of global production capacity for A (H1N1) pandemic vaccine”
Capacity may become available November in the best case, but may not materialize before April 2010

Surplus H1N1 Capacity Available from High-Income Country Facilities¹
- Assuming 1:1 yields and no 2010-11 seasonal production

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Doses Produced</th>
<th>Surplus Doses to July 2010</th>
<th>Date Contracts Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 09</td>
<td>4.2B</td>
<td>3.3B</td>
<td>November 09</td>
</tr>
<tr>
<td>February 10</td>
<td>4.2B</td>
<td>2.4B</td>
<td>February 10</td>
</tr>
<tr>
<td>January 10</td>
<td>2.5B</td>
<td>1.6B</td>
<td>January 10</td>
</tr>
<tr>
<td>April 10</td>
<td>2.5B</td>
<td>0.7B</td>
<td>April 10</td>
</tr>
</tbody>
</table>

Source: WHO survey
1 Assumes all facilities switch to H1N1 production at end of July (however, in reality, some facilities are converting earlier)

Source: Marie-Paule Kieny, WHO, presentation titled “Assessment of global production capacity for A (H1N1) pandemic vaccine”
Proposed Principles for Consideration I

- The global community should take steps to protect all populations, including those without resources to protect themselves.
- Vaccination should be considered in the context of comprehensive pandemic preparedness and response efforts in all nations.
- Developed countries and vaccine manufacturers should urgently establish a priori agreement on a mechanism to ensure access to vaccine by developing countries.
- Influenza vaccine manufacturers should identify strategies such as tiered pricing and/or donations to make pandemic vaccine more accessible to developing nations.

“Principles discussed at a meeting hosted by the Bill & Melinda Gates Foundation on June 18, 2009. Participants included representatives of the WHO, developed and developing countries, vaccine manufacturers and regulatory authorities.”
Proposed Principles to Consider II

- Pandemic vaccines allocated to developing nations should become available in the same timeframe as vaccine for developed nations.
- The global community should seek to establish a consensus on the safety and efficacy of adjuvants, and efforts should be made to ensure the fullest use of this and other dose sparing strategies.
- All countries obtaining pandemic vaccine should ensure that mechanisms are in place to provide this vaccine to their populations and to ensure that this scarce resource is not wasted.
- The World Health Organization is uniquely positioned to lead the global response to a pandemic virus.

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