Epidemiology of Seasonal and Pandemic Influenza Vaccination

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Epidemiology of Seasonal and Pandemic Influenza Vaccination

Seasonal Influenza Vaccination Before the 2009 H1N1 Pandemic

Many of these slides were obtained from presentations made at WHO’s Second Consultation on the Global Action Plan for Influenza Vaccines (GAP-II) held in Geneva on 12-14 July 2011

Seasonal Influenza Vaccination in 71 MIVSG Countries, 2002-2005

Doses of influenza vaccine distributed / 1000 population

Vaccine-producing

Non-producing

2002
2005
Implications (in 2007) of the MIVSG Findings for Pandemic Vaccination

- Global vaccine distribution had increased from 292 M doses in 2003 to >329 M in 2005
- ~95% of all doses were produced in 9 countries
- In 2005, these 9 countries had 12% of the world’s population and used 59% of doses of vaccine
- Steady growth in vaccine use continued in non vaccine-producing countries outside Western Europe, Canada and the US

Tam T, Fedson DS. *Options for the Control of Influenza VI*. Int Med Press 2008, pp189-91 and unpublished observations
Implications (in 2007) of the MIVSG Findings for Pandemic Vaccination

• Through 2009, all non vaccine-producing countries, including all countries in Latin America, imported virtually all of their vaccines from five Western European countries

• In 2007, the UN System Influenza Coordinator reported that almost 100 countries would want to be supplied with pandemic vaccines

• In the event of a severe pandemic, vaccine producing countries might not allow the export of pandemic vaccines to non-producing countries, leading to a global political as well as public health crisis
WHO Countries Recommending Seasonal Influenza Vaccination, 2008-09

WHO Global Action Plan - II, 12-14 July 2011
Distribution of Seasonal Influenza Vaccine by WHO Region, 2004-2009
Seasonal Influenza Vaccine Coverage Among Elderly Persons in Europe, 2007/08

WHO Global Action Plan - II, 12-14 July 2011
Seasonal Vaccine Coverage ≥ 65 Yrs and Reimbursement Policies in 29 European Countries, 2008

US Influenza Vaccine Supply
Cumulative Number of Doses
2004/05 - 2010/11 Influenza Seasons

WHO Global Action Plan - II, 12-14 July 2011
Seasonal Influenza Vaccine Distribution and Coverage in Brazil, 1999-2111

Doses distributed

% coverage ≥60y

Doses ↓

2088 - Coverage target increased from 70% to 80%
Seasonal Influenza Vaccination Coverage Among the Elderly in Selected Latin American Countries

WHO Global Action Plan - II, 12-14 July 2011
Seasonal Influenza Vaccine Income and Doses Distributed by Province in China, 2005-5 to 2008-9

• Estimated target population - 571 M (43%)
• Vaccine companies - 11 domestic and 5 multinational
• Doses distributed
  - 2004-5 - 17 M
  - 2008-9 - 32.5 M
Domestic production capacity in 2009 - 126 M doses

WHO Global Action Plan, 11 June 2011
Seasonal Influenza Vaccine Distribution in 157 Countries in 2009

TOP 10
- Netherlands
- Qatar
- France
- Spain
- Italy
- UK
- Germany
- Belgium
- Chile
- Rep. of Korea

WHO Global Action Plan - II, 12-14 July 2011
Global Distribution of Seasonal Influenza Vaccine, 2004-2009

Seasonal Distribution has been steadily increasing, however this is slowing as ‘saturation’ of current seasonal markets is reached.

WHO Global Action Plan - II, 12-14 July 2011
Epidemiology of Seasonal and Pandemic Influenza Vaccination

The H5N1 Pandemic Threat
The H5N1 Pandemic Threat: Why We Were Worried

- Avian (H5N1) influenza in humans had killed ~60-80% of those infected (since 2003)

- Recent population die-offs in mammals
  - early 1980s, avian (H7N7) influenza killed 20% of the harbour seals along the North Atlantic coast
  - early 1990s, distemper killed ~ 1/3 of the lions in East Africa
  - early 2000s, Ebola virus has killed ~ 50% of the gorillas and chimps in several regions of Central Africa

For the influenza virus, human beings are bystanders; our disappearance would not affect its survival in nature
Estimated Global Mortality of a 1918-like Pandemic in 2004

- Excess mortality estimates in 1918-1920 varied > 30-fold across countries
- > 50% of this variation was explained by per capita income
- A similar pandemic in 2004 would have killed 62 million (51-81 million) worldwide
- 96% of deaths would have occurred in developing countries
- Historians estimate the 1918 pandemic was much worse - 50-100 million deaths worldwide

Influenza Virus Genetic Reassortment: The Possibility of a Much More Severe Pandemic Has Not Gone Away

In an experiment published in 1974, co-infection of susceptible turkeys with two influenza viruses, one benign and one high path, generated a new reassortant virus that killed all of the infected birds and all of their contacts → a total population collapse!

WHO press conference 23 May 2007

“The world is not prepared for a pandemic … we don’t have enough vaccine”… (we can cover only 1.5 billion people), and it will be … “a five year maximum before we believe we will have enough vaccine to begin to talk about equitable sharing.”

World Health Assembly resolution follow up

40-60 M dose vaccine stockpile will cover only HCWs and VIPs

WHO press statement on 16 May 2007

four-year $58 M program for yellow fever vaccination for 48 million people in West Africa. Yellow fever accounts for 30,000 deaths in this region each year.
The ‘Unforgiving Arithmetic’ of H5N1 or H1N1 Pandemic Vaccine Supply: An Example from the U.S.

• Domestic vaccine requirement - 1 or 2 doses of inactivated vaccine for every person (ideal !)
  $300 \text{ M people} \times 1 \text{ or} 2 \text{ doses} = 300 - 600 \text{ M doses}$

• Domestic vaccine production capacity increased in 2009
  $150 \text{ M doses of trivalent vaccine per year} \rightarrow 450 \text{ M doses of monovalent pandemic vaccine per year} @ 15 \mu g \text{ HA per dose} \rightarrow 75 \text{ M doses could be produced in 2 months!}$

• The pandemic vaccine challenge → develop and produce an adjuvanted vaccine containing
  - $1.875 \mu g \text{ HA / dose if two doses per person} (75 \times 15 / 600)$
  - $3.75 \mu g \text{ HA / dose if one dose per person} (75 \times 15 / 300)$

Clinical Trials of Inactivated H5N1 Vaccines in the US and Other Countries: 2004 - 2009

- FDA favored non adjuvanted vaccines → NIAID trials that showed two 90 μg HA non adjuvanted doses were moderately immunogenic
- In early 2009, 6 months’ domestic production would have been enough to vaccinate < 5% of the US population → a national vaccination program that would have been socially and politically unsustainable
- The US has not yet tested any adjuvanted H5N1 (or H1N1) vaccine
- In Europe, 2 doses of proprietary adjuvanted split virus H5N1 vaccine (1.9 μg HA - Sanofi Pasteur and 3.75 μg HA -GSK) met EMEA/CHMP registration criteria
- In China (Sinovac - 10 μg HA ) and Japan (4 companies - 5 μg HA, 2 doses of alum adjuvanted, whole virus vaccine were tested
- In Australia (CSL- 30 μg HA) 2 doses of alum adjuvanted, split virus vaccine were tested

### Pandemic H5N1 Vaccination for an Individual or a Population?

<table>
<thead>
<tr>
<th>µg HA per dose</th>
<th>Individual</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% with neut Ab $\geq 1:40$</td>
<td>Number of people Vaccinated</td>
</tr>
<tr>
<td>90</td>
<td>54</td>
<td>100</td>
</tr>
<tr>
<td>45</td>
<td>43</td>
<td>200</td>
</tr>
<tr>
<td>15</td>
<td>22</td>
<td>600</td>
</tr>
<tr>
<td>7.5</td>
<td>9</td>
<td>1200</td>
</tr>
</tbody>
</table>

Registering Adjuvanted Pandemic Vaccines: US and European Criteria

• FDA criteria have focused on the individual, not the population
  “… the immune response elicited by the adjuvanted antigen (should be) significantly better than that elicited by the same antigen alone.” A two-fold increase in HI antibody or a 15% increase in seroconversion rate will be considered a meaningful difference (Draft, March 2006)

• Europe - all three CHMP criteria for immunogenicity and safety must be met - “mock-up” dossier

When supplies are limited and demand is great, pandemic vaccines that meet the needs of populations become essential
NIH-funded vaccine trials involved
- 6200 children, younger and older adults
- 4 different vaccine companies
- 3 dose levels
- one and two doses

In immunologically naïve subjects, large doses of whole virus vaccine were required and two doses were better than one.

Within 4-5 months of isolating the swine influenza virus, publicly funded studies had determined the vaccine formulation and vaccination schedule.

A Political Crisis Emerged in 2007
Before the H1N1 Pandemic

• In February 2007, Indonesia announced it would no longer share its H5N1 viruses with WHO unless it could have access to affordable pandemic vaccines

• World Health Assembly resolution in May 2007 attempted to address this problem
  - transfer production technology to six developing countries ($20 million)
  - create international stockpile of pandemic vaccines
  - establish mechanism for vaccine financing
  - renegotiate ‘terms of reference’ for virus sharing

• The impasse between Indonesia and WHO over virus sharing was not “resolved” until May 2011
Status of H5N1 Vaccine Development in Early 2009, Before the H1N1 Virus Emerged

• The global demand for pandemic H5N1 vaccines was expected to be > 4-8 billion doses
• Demand for seasonal vaccines was increasing too slowly
• RG-engineered H5N1 viruses had given poor yields
• Egg- and cell-based production capacity was not expected to increase substantially before 2011-2012
• Vaccine companies had made conservative decisions in developing their own adjuvanted H5N1 vaccines
• Government funding for clinical trials was generous in the US, but almost non existent in Western Europe
• Almost all new vaccines and vaccination technologies (LAIV, ID delivery, recombinant HA, dermal patches, virosomes, DNA vaccines, etc.) were certain to take many years to develop and be registered
Epidemiology of Seasonal and Pandemic Influenza Vaccination

The H1N1 Pandemic in 2009-10
The H1N1 pandemic was not the pandemic we were preparing for!
The H1N1 Pandemic and Clinical Trials of H1N1 Vaccines

- A new H1N1 virus was identified in late April, and within a few months the “first wave” of infection had spread throughout the world.
- In the Northern Hemisphere, the “second wave” was largely over in late December, ~8 months later.
- The epidemiologic impact was mild, older adults were protected because of previous natural exposure to H1N1 viruses (and vaccines), but 30-50% of children and younger adults were infected.


- Several clinical trials showed that 95-100% of persons ≥9 yrs given only one dose of non adjuvanted H1N1 vaccine produced anti-HA antibodies levels ≥1:40.

The WHO Global Action Plan (2006) anticipated 2 B doses of pandemic vaccine would be produced within 6 months, yet only 534 M doses (27%) of H1N1 vaccine were actually produced.

**H1N1 Vaccine Production in 2009-2010**

**Global Forecast and Actual Production**

<table>
<thead>
<tr>
<th></th>
<th>Doses forecasted (M)</th>
<th></th>
<th>Actual production (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>June 2009</td>
<td>Jan 2010</td>
<td></td>
</tr>
<tr>
<td>1 December 2009</td>
<td>2459</td>
<td>--</td>
<td>534</td>
</tr>
<tr>
<td>Adjuvanted</td>
<td>--</td>
<td>--</td>
<td>169</td>
</tr>
<tr>
<td>Non-adjuvanted</td>
<td>--</td>
<td>--</td>
<td>342</td>
</tr>
<tr>
<td>Live-attenuated</td>
<td>--</td>
<td>--</td>
<td>23</td>
</tr>
<tr>
<td>1 March 2010</td>
<td>3689</td>
<td>1303</td>
<td>--</td>
</tr>
<tr>
<td>1 June 2010</td>
<td>4918</td>
<td>1367</td>
<td>--</td>
</tr>
<tr>
<td>Seasonal NH 2009</td>
<td>493</td>
<td>--</td>
<td>500</td>
</tr>
<tr>
<td>Seasonal SH 2010</td>
<td>112</td>
<td>73</td>
<td>--</td>
</tr>
</tbody>
</table>

342 M doses of non adjuvant vaccine (15 \( \mu g \) HA) → 1.37 B doses of adjuvanted vaccine (3.75 \( \mu g \) HA)

**AN ADDITIONAL 1 BILLION DOSES!**

Global Pandemic Vaccine Production in 2009-10: Planned vs Actual

WHO Global Action Plan - II, 12-14 July 2011
The H1N1 Pandemic in the US: A Race Between the Virus and the Vaccine

WHO Global Action Plan - II, 12-14 July 2011
Evolution of the H1N1 Pandemic in the US and Delivery of H1N1 Vaccines

The second wave of the H1N1 pandemic “peaked” in early December when only ~75 M doses of vaccine had been delivered. At this time, Mexico received its first 860,000 doses of pandemic vaccine.

http://www.cdc.gov/h1n1flu/vaccination/vaccinesupply.html

<table>
<thead>
<tr>
<th>Date</th>
<th>Oct 17</th>
<th>Nov 20</th>
<th>Dec 12</th>
<th>Dec 31</th>
<th>Jan 16</th>
<th>Jan 29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doses (M)</td>
<td>8.0</td>
<td>45.8</td>
<td>76.4</td>
<td>99.4</td>
<td>115.5</td>
<td>118.9</td>
</tr>
</tbody>
</table>
H1N1 Vaccination Rates in Developed Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Seasonal 2007 (%)*</th>
<th>% H1N1 2009-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>47</td>
<td>24</td>
</tr>
<tr>
<td>Canada</td>
<td>33</td>
<td>40</td>
</tr>
<tr>
<td>Australia</td>
<td>23</td>
<td>30</td>
</tr>
<tr>
<td>UK</td>
<td>27</td>
<td>7</td>
</tr>
<tr>
<td>Germany</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>Italy</td>
<td>24</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Spain</td>
<td>24</td>
<td>?</td>
</tr>
<tr>
<td>France</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>Ireland</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Poland</td>
<td>6</td>
<td>none</td>
</tr>
<tr>
<td>China</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

* www.ifpma.org

- Little country-specific information on number of vaccine doses purchased and administered
- Substantial numbers vaccinated in the US, Canada and Australia
- Low rates in Western Europe due to concern about vaccine safety (adjuvants) and opposition by anti-vaccine groups
- Millions of doses unused → contracts renegotiated and doses returned, donated or destroyed
- Political outcry based on alleged overselling of the pandemic threat and antagonism toward profiteering vaccine companies and WHO
Latin American Countries That Planned to Obtain Supplies of H1N1 Vaccines

PAHO report, 3 May 2010
Time Differences in Access to Pandemic Vaccines in the Americas

WHO Global Action Plan - II, 12-14 July 2011
Pandemic Vaccine Coverage Rates in Target Groups in Latin America

144 million people vaccinated: 98% coverage in LAC

WHO Global Action Plan - II, 12-14 July 2011
Pandemic Vaccine Coverage Rates in Specific Target Groups in Latin America

Coverage >100% reflects problems with denominator estimation

WHO Global Action Plan - II, 12-14 July 2011
Deaths From the H1N1 Pandemic in Latin America

- In Latin America, the first and second pandemic waves were over by January 2010, and there was very little additional influenza activity through late 2010
- Very few doses of H1N1 vaccine had reached any of these countries by January 2010

Regional Incidence of Pandemic (H1N1) Influenza in Brazil, 2010

Incidence /1 million hab. (n=973)

WHO Global Action Plan - II, 12-14 July 2011
H1N1 Vaccination Rates in Selected Latin American Countries

- Latin American countries obtained H1N1 vaccine from 3 sources
  - country purchases (140 M)
  - PAHO Revolving Fund (20M)
  - WHO donations (7M)
- On 3 May 2010, PAHO estimated that 70M people in LAC had received H1N1 vaccine
- Accurate and comprehensive country-specific estimates of the number of vaccine doses supplied and administered are unobtainable
- H1N1 vaccine surpluses reported in many LAC

<table>
<thead>
<tr>
<th>Country</th>
<th>Seasonal 2007 (%)</th>
<th>% H1N1 2009-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chile</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td>Mexico</td>
<td>16</td>
<td>?</td>
</tr>
<tr>
<td>Cuba</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>El Salv.</td>
<td>16</td>
<td>31</td>
</tr>
<tr>
<td>Brazil</td>
<td>12</td>
<td>?</td>
</tr>
<tr>
<td>Paraguay</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Argentina</td>
<td>9</td>
<td>?</td>
</tr>
<tr>
<td>Venezuela</td>
<td>6</td>
<td>none</td>
</tr>
<tr>
<td>Honduras</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Peru</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

*www.ifpma.org*
Conclusions of the Fineberg IHR Report (May 2011)

- local and national core capacities called for in the IHR are not fully operational and are not now on a path to timely implementation worldwide
- WHO performed well during the pandemic, confronted systemic difficulties and demonstrated some shortcomings, but there was no evidence of malfeasance
- the world is “ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public health emergency”
- need for “research, strengthened health-care delivery systems, economic development in low- and middle-income countries and improved health status ”

WHO Global Action Plan - II, 12-14 July 2011
Recommendations of the Fineberg IHR Report for a WHO pandemic preparedness response
- strengthen internal capacity for a sustained response
- improve practices for appointing an emergency committee
- revise pandemic preparedness guidance
- develop and apply measures to assess severity
- streamline management of guidance documents
- implement a strategic, organization-wide communications policy
- encourage advance agreements for vaccine distribution and delivery

WHO Global Action Plan - II, 12-14 July 2011
Recommendations of the Fineberg IHR Report for a global response

- establish a more extensive global, public health reserve workforce
- create a contingency fund for public health emergencies
- reach agreement on the sharing of viruses and access to vaccines and other benefits
- pursue a comprehensive influenza research and evaluation program

WHO Global Action Plan - II, 12-14 July 2011
Two Fundamental Requirements for Global Pandemic Vaccination

- **Antigen sparing vaccines**
  - high growth reverse genetics seed strain
  - inexpensive universally available adjuvant
  - formulation suitable for populations, not just individuals

- **Effective management**
  - government funding of vaccine development
  - resolution of IP and liability issues
  - rapid production of huge amounts of vaccine
  - international organization and management of vaccine production, financing, distribution and administration

Were The Fundamental Requirements Met for H1N1 Pandemic Vaccination?

• Antigen sparing vaccines
  - Reverse genetics failed to deliver a high growth H1N1 seed strain
  - the only effective adjuvants were proprietary and expensive, and their costs and unfounded safety concerns contributed to the lack of interest in adjuvanted H1N1 vaccines in Europe and other countries
  - FDA’s decision to not license adjuvanted vaccines reflected a concern for individuals, not populations, and it dramatically reduced the number of doses that were produced

• Effective management
  - except for the US and China, there was no government funding for vaccine development
  - IP issues for adjuvants were not challenged, although almost all countries receiving vaccines accepted responsibility for liability
  - rapid production of huge amounts of vaccine was not achieved
  - except for limited WHO involvement, there was no international organization and management of vaccine production, financing and distribution
Epidemiology of Seasonal and Pandemic Influenza Vaccination

Estimates of Future Influenza Vaccine Production Capacity and Demand
## Seasonal Influenza Vaccine
Projected Demand and Supply (IFPMA)

<table>
<thead>
<tr>
<th>Year</th>
<th>Demand:</th>
<th>(theoretical) Global production capacity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>449 million*</td>
<td>876 million **</td>
</tr>
<tr>
<td>2015</td>
<td>Depends on national policies and their implementation</td>
<td>1.764 billion **</td>
</tr>
</tbody>
</table>

WHO Global Action Plan - II, 12-14 July 2011
Expansion in Production Capacity Will Still Not Allow Developing Countries to Have Timely Access to Pandemic Vaccines

Future production capacity (2008 – 2016)
Seasonal doses per year, assuming 10 months of operation

WHO Global Action Plan - II, 12-14 July 2011
Influenza Vaccine Production Capacity in Developing Countries

WHO Global Action Plan - II, 12-14 July 2011
Estimated Pandemic Vaccine Production Capacity in 2015

WHO Global Action Plan - II, 12-14 July 2011
Projected Seasonal Vaccine Production Capacities and Demand, 2007-2014 (IFPMA)

WHO Global Action Plan - II, 12-14 July 2011
New Approaches Are Needed
Recombinant HA (rHA) Vaccines

- An rHA seasonal vaccine is known to be safe and immunogenic
- Efficacy is ~100% against culture-proven influenza and 54% efficacious against ILI, despite vaccine/circulating virus mismatch
  

- FDA has still not licensed a seasonal rHA vaccine in the US
- An adjuvanted rHA pandemic vaccine could be developed, but the company did not receive government support until mid-2009, after the H1N1 pandemic virus emerged

rHA pandemic vaccines could be produced in pharmaceutical bioreactors, and the existing global bioreactor capacity is 2M liters

Number of People Vaccinated With Egg-based or rHA Adjuvanted Pandemic Vaccines - 2007 Estimate*

<table>
<thead>
<tr>
<th>No. of months of production</th>
<th>Conventional egg-based vaccine</th>
<th>rHA vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 µg HA (no adj)</td>
<td>29.4 M</td>
<td>283 M</td>
</tr>
<tr>
<td>3.75 µg HA (with adj)</td>
<td>117 M</td>
<td>1.1 billion</td>
</tr>
<tr>
<td>Three</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 µg HA (no adj)</td>
<td>88 M</td>
<td>.83 billion</td>
</tr>
<tr>
<td>3.75 µg HA (with adj)</td>
<td>350 M</td>
<td>3.4 billion</td>
</tr>
</tbody>
</table>

*Assumes production yields similar to seasonal vaccines and two doses per person

New Approaches Are Needed
Live-attenuated Influenza Vaccines

Live-attenuated influenza vaccine (LAIV) for seasonal intranasal vaccination was licensed in the US in 2000 (MedImmune/AstraZeneca)

Advantages of LAIVs for pandemics
- broad cross-protection in mice and ferrets
- one-dose, needle-free administration

Pre-pandemic use not possible, although LAIV could be stockpiled
LAIV production capacity is limited, but highly efficient

Increased egg-based capacity

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Increased Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated whole virus</td>
<td>3-fold</td>
</tr>
<tr>
<td>Inactivated + adjuvant (oil-in-water)</td>
<td>6-12-fold</td>
</tr>
<tr>
<td>LAIV</td>
<td>≥50-100-fold</td>
</tr>
</tbody>
</table>

In 2009, several billion doses of LAIV could have been produced in a few months in the egg-based production facilities that were used to produce inactivated vaccines

LAIV Production Timeline for Pandemic Vaccine, 2009

2009 H1N1 Pandemic LAIV Timeline

- Received 2 Swine Flu Isolates
  - April
- LAIV Vaccine Seed Prepared
  - June
  - Begin Bulk Manufacturing (90 doses per egg)
  - July
- Clinical Trials Start
  - August
- FDA Approval
  - September
- Shipping Starts
  - October
- Vaccination Starts
  - November

- LAIV was first pandemic vaccine shipped to the US government
  - Provided ~25% of US doses
  - Significant use by children

WHO Global Action Plan - II, 12-14 July 2011
Estimated LAIV Production Times in Eggs and Cell Culture

- Time from strain ID to seed generation unchanged
- Time to produce bulk vaccine reduced by 2 or more months

![Graph showing estimated LAIV production times in eggs and cell culture]
Confronting Influenza Pandemics
Can They Be Successfully Managed?

“The ‘sound’ banker ... is not one who sees danger and avoids it, but one who, when he is ruined, is ruined in a conventional and orthodox way along with his fellows so that no one can really blame him.”

John Maynard Keynes

“It is not enough to say, 'We are doing our best.' You have got to succeed in doing what is necessary.”

Winston Churchill

“Try again, fail again, fail better.”

Samuel Beckett

Worstward Ho 1983
Thank you!
References

• Fedson DS. Vaccine development for an imminent pandemic: why we should worry, what we must do. *Hum Vac* 2006; 2: 38-42.
• Fedson DS. Confronting the next influenza pandemic with anti-inflammatory and immunomodulatory agents: why they are needed and how they might work. *Influenza Other Respir Virus* 2009; 3: 129-42.

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