The International Dimension of the Regulatory Response to the H1N1 Pandemic

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Outline

- Vaccines – pandemic context
- International regulatory preparedness
- Surprise…H1N1!
- International collaboration as part of the regulatory response to H1N1 (2009) pandemic
- Lessons learned
Vaccines – pandemic context

• Vaccines play a key part in national and global pandemic plans

• The likelihood, timing, and spread of a pandemic is unknown - vaccine cannot be developed until pandemic strain isolated

• Development timelines critical in the face of rapidly emerging epidemic/pandemic

• Strategies to shorten the time between emergence of a human pandemic influenza virus and availability of safe and effective vaccines are of highest priority
Regulatory preparedness

• Inter-pandemic period used to explore optimal strategies (quality, clinical, regulatory) for developing and licensing pandemic influenza vaccines

• Develop regulatory pathways to enable authorization and use of vaccine which do not meet normal regulatory requirements

• Develop scientific basis for making regulatory decisions for pandemic influenza vaccines…involves large science component

➢ Global issue which called for proactive, global collaboration
HUMAN VACCINES FOR PANDEMIC INFLUENZA

REGULATORY PREPAREDNESS WORKSHOPS

WORKSHOP 1: Ottawa, 9-11 March 2006
WORKSHOP 2: Bethesda, 12-13 June 2006
WORKSHOP 3: Geneva, 14-15 June 2007
International Regulatory Preparedness

• Between 2006-2007, 3 technical workshops were held with representation of NRAs from vaccine producing countries and those exploring influenza vaccine production

✓ Created a global network of regulatory authorities engaged in pandemic influenza vaccine regulation
✓ Resulted in joint development of WHO regulatory preparedness guidelines
✓ Identified gaps/areas of regulatory uncertainty
✓ Led to regulatory cooperation
WHO Regulatory Guidelines

• Regulatory preparedness for human pandemic influenza vaccines (2007)

• Provides NRAs and vaccine manufacturers with advice on regulatory pathways, considerations for evaluation of quality, safety and efficacy, and requirements for post-marketing surveillance

• Scope includes live attenuated and inactivated vaccines:
  (1) vaccines against novel human influenza viruses (‘mock’ vaccines),
  (2) vaccines intended for stockpile, and
  (3) subsequent pandemic influenza vaccines

• Evolving field; therefore, it was to be considered a “living document”
Key Regulatory Challenges Identified

- Clinical evaluation for safety/efficacy difficult in absence/low level disease or if infection remains focal in nature
- Not possible to follow traditional regulatory process
- Challenge to ensure public safety / not inhibit development and access to vaccine
- Clinical trials / licensing in children and other population groups
- Stockpile issues
Key Regulatory Challenges Identified

• Appropriate regulatory pathways and criteria for vaccine licensing
  • Also important for pre-qualification of pandemic vaccines

• Timing of availability of vaccine candidate strain and reference reagents for quality control

• Regulatory capacity and preparedness to perform batch release

• Limited data on safety at time of licensure – plans for post-market surveillance for vaccine safety and effectiveness
A pandemic could be declared at any point

As much data as possible to be collected in inter-pandemic period so that pandemic vaccine can be licensed with minimal additional data

*Contingency needed in the event that the pandemic strain differs significantly from the strain in the vaccine against novel human influenza virus. If this is the case, data may be of little value for extrapolation to use with the pandemic strain.

Most ‘mock’ vaccines manufactured with H5N1 strain
Surprise…H1N1!

• Much different from ‘mock’ H5N1 vaccines produced in the pre-pandemic period
  • Will H1N1 behave similar to H5 or more like seasonal viruses?
  • Will one or two doses be needed? (two adjuvanted doses of H5N1 vaccine were needed to induce an immune response)

• Emergence of virus in North America in April
  • Differs from assumptions made in pandemic planning – less time to respond
International Collaboration

World Health Organization

- Biweekly teleconferences with global network of influenza vaccine regulators
  - Continuation of network responsible for drafting WHO regulatory preparedness guidelines

- Weekly safety surveillance teleconferences once H1N1 vaccines were rolled out

- WHO also held regular teleconferences with manufacturers

  Agreement to share data and information on potential adverse events in real-time
International Collaboration

- Other bilateral and multilateral working relationships, on a routine or ad-hoc basis

- For example, Health Canada-EMA-FDA set up regular teleconferences to discuss regulatory issues; focus was on vaccines being filed in all three jurisdictions.
  - **Core group** to discuss broader regulatory issues (EMA-FDA-HC)
  - **Clinical development** sub-working group (EMA-FDA-HC)
  - **Pharmacovigilance** sub-working group (multiple regulators, including Australia and Japan)
International Collaboration

• Regulatory capacity to perform vaccine lot/batch release in a pandemic situation was identified as an issue in the pre-pandemic period

• During the pandemic, NRAs of manufacturing companies played an important role in lot release, particularly for markets to which H1N1 vaccines were sold or donated, without capacity to do their own testing
Benefits of International Collaboration

• Data were shared in real-time
• Maximized amount of data/knowledge available to support regulatory-decision making/licensure
• Northern Hemisphere learned from vaccine experience in Southern Hemisphere
• Opportunity to harmonize requirements (e.g. NRA consensus that clinical trials would not be needed if higher yielding strain (antigenically similar) became available)
• Regular updates on vaccine strains and potency testing reference reagents
Lessons learned

• Regulatory preparedness and real-time collaboration were essential to help ensure quick access to safe and effective vaccines in the event of a pandemic

• Previously established global network of influenza vaccine regulators provided a useful forum for information-sharing amongst NRAs
  • Propose/recommend that this type of model be used in future public health crises

• Even though there were regional differences, bilateral and trilateral information exchanges were useful
Lessons Learned

• Preparedness initiatives need to consider other strains with pandemic potential – H1N1 caught us by surprise

• Build in plans to collect data on certain target sub-groups (e.g. pregnant women, children)

• Pandemic experience enabled us to identify where MOUs/information-sharing agreements may be needed
Lessons Learned

• We can develop better strategies for communicating on certain issues, such as the role of the regulator and other key players, use of adjuvants, etc. The level of communications was underestimated.

• Influenza vaccine production capacity limited globally
  • Any initiatives to increase production capacity need to be accompanied by regulatory capacity-building initiatives
Lessons Learned

• Traditional potency assay (SRID) – potential for challenges or delays in preparation, standardization and distribution of reference reagents in a pandemic situation. Priority should be given to continuing research and development on alternative assays.

• This is something that individual regulators cannot address independently; it requires global collaboration and considerable scientific research

• July 2010 Potency Testing Workshop is a good example of continued international collaboration in this area
Questions?