Vaccines and Associated Regulatory Issues relevant in the Pandemic Context

Catherine Parker
Biologics and Genetic Therapies Directorate
Health Canada
Outline

• Vaccines – Pandemic Context
• International Regulatory Preparedness
• Key Regulatory Challenges/Issues
• Importance of Regulatory Cooperation
• Conclusions/Path Forward
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 strain is unknown until pandemic declared
• Development timelines are 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 to be used to explore optimal strategies (quality, clinical, regulatory) for developing and licensing pandemic influenza vaccine
- Develop regulatory pathways to enable authorization and use of vaccine which do not meet normal requirements
- Involves large science component
- Developing scientific basis for making regulatory decisions for pandemic influenza vaccines
  ➢ Global issue
International Regulatory Preparedness

- Science, commerce and public health concerns in vaccine field are truly international
- Regulations in place in all developed countries to ensure regulatory oversight of vaccines prior to and after licensing
- Appropriate control measures are essential to safeguard against unacceptable adverse events and ineffective vaccines
- Decisions on regulation and testing increasingly need to be made internationally
  - Vital for pandemic influenza vaccine since new products/new manufacturers
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 regulatory guidelines – promotion of regulatory convergence
✓ Identified gaps/areas of regulatory uncertainty
✓ Lead to regulatory cooperation
WHO Regulatory Guidelines

- Regulatory Preparedness for Human Pandemic Influenza Vaccines
- 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,
  (2) vaccines intended for stockpile, and
  (3) Subsequent pandemic influenza vaccines
- Evolving field; therefore, it is considered a “living document” that will be updated as knowledge gained
Key Regulatory Challenges/Issues

- 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
Key Regulatory Challenges/Issues

• Appropriate regulatory pathways and criteria for vaccine licensing

• Stockpile issues

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

• Regulatory capacity and preparedness to perform batch release

• Post-marketing surveillance for vaccine safety and effectiveness
Regulatory Pathways

• Facilitate necessary pathways for vaccine licensing
• Closer interaction between NRAs and manufacturers and between NRAs is required, especially in emergency use situations
• Convergence of regulatory pathways between NRAs could help WHO prequalification and facilitate the availability of vaccine on a global scale
  • Requires information-sharing agreements, agreement on core data requirements
  • WHO Regulatory Guidelines provide recommendations pertaining to quality, non-clinical, clinical specifications and post-market surveillance
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, the data may be of little value for extrapolation to use with the pandemic strain
Emergency (Early) Access

• Many NRAs have a number of regulatory mechanisms in place that could provide, if necessary, early access to vaccine if normal conditions of authorization have not been met

• Existing laws and regulations within jurisdictions may restrict options for emergency use – countries to review their options and implement any corrective measures

• The data available at the time of a pandemic will dictate which emergency use option is most suitable

• Vaccines against novel human influenza viruses may be the only vaccines available to those most affected early in a pandemic
Vaccine Stockpiles

• Country-level decision to establish a national stockpile in anticipation of an influenza pandemic

• WHA Resolution 60.28 urges WHO to establish an international stockpile of H5N1 vaccine or other influenza vaccines based on influenza viruses of pandemic potential
  1. For rapid response to a pandemic signal
  2. To provide assistance to countries that otherwise would be without access to vaccine to enable vaccination of selected parts of the population considered to be critical to maintain functionality of the country

• WHO to develop transparent rules and procedures for its operation, including its regulatory oversight
H5N1 Vaccine Stockpile - Regulatory Considerations

• Different from existing stockpiles that consist of well-known products with established safety/efficacy profiles
• WHO consultation on technical specifications held in October 2007
• Operation and oversight will be challenging
  ➢ Continued appropriateness of the H5 strain in the stockpiled vaccine
  ➢ Continued suitability of the potency of the vaccine; well-defined stability testing program needed
  ➢ Interchangeability of stockpile vaccines - clear selection criteria to be developed to simplify stockpile management; only inactivated influenza vaccines to be accepted based on current evidence
  ➢ What to stockpile – bulk antigen, final formulated product, final product?
H5N1 Vaccine Stockpile - Regulatory Considerations

- Roles and responsibilities for oversight and ongoing data collection need to be defined

- Recommendation that stockpiled vaccines be WHO pre-qualified

- Evolving area - flexibility about data requirements to be retained
WHO Pre-qualification

• Proposed for vaccines against novel human influenza viruses and pandemic vaccines
• Enhance level of regulatory confidence in an influenza vaccine in the event of a pandemic and enhance vaccine availability
• Vaccines for international stockpile to be pre-qualified
  • Requires that vaccines against novel human influenza virus be licensed by the NRA of the producing country
  • These vaccines have already been licensed in some countries; in others they have not
  • WHO criteria may differ from country licensing criteria; early discussion with NRAs is essential
Availability of Strain and Reagents

• Issues related to rapid availability of vaccine production strains & reference reagents for quality control

• Once strain identified, there may be difficulty (globally) to get enough reagents to determine quality control requirements to support licensure

• Importation issues for pandemic strain and reagents
Batch Release

- Regulatory capacity and preparedness to perform vaccine batch release
- Identify ways to streamline batch release procedures
- Build mutual confidence between regulatory authorities of different countries
Importance of Regulatory Cooperation

- Production of vaccine strain and reagents - streamline process
- Making reagents available globally
- Lot release – global markets
- Regulatory research /assays
- Sharing information and regulatory expertise

➢ Regulatory Network established
Post-marketing Surveillance

- **Limited data on safety** at time of licensure - monitoring safety post-marketing

- A plan needs to be in place to monitor vaccine safety and to ensure the timely communication of any potential adverse event following immunization (AEFI) during the pandemic.
Other Related Issues

• Regulators must develop plans to address the following prior to and during a pandemic:
  • Business continuity
  • Continued release of other ‘non-pandemic influenza’ vaccines
  • Uses for vaccines against novel influenza viruses developed during inter-pandemic period
  • National stockpiles, donation to international stockpiles, preparedness to accept vaccine from international stockpiles
Conclusions/Path Forward

• Regulatory preparedness and cooperation are essential to help ensure quick access to a safe and effective vaccine in the event of a pandemic

• Evolving field; continued regulatory collaboration and cooperation is essential
  • Regulatory Network is already established

• Process for information-sharing between manufacturers, NRAs, and developing countries to maximize successful vaccine production