Facilitating Development of and Access to New Vaccines: An FDA Perspective

Karen Midthun, MD, Deputy Director
Center for Biologics Evaluation and Research, FDA
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Topics for today

- CBER vision, mission, selected public health accomplishments
- CBER role in facilitating development, availability, and licensure of vaccines
- CBER vaccine initiatives and guidances

Vision for CBER

INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- **Protect and improve public and individual health in the US and, where feasible, globally**
- **Facilitate the development, approval and access to safe and effective products and promising new technologies**
- **Strengthen CBER as a preeminent regulatory organization for biologics**

Biological Products Regulated by CBER

- Vaccines (preventive and therapeutic)
- Blood, blood components and derivatives
- Allergenics
- Cell and Gene Therapies
- Tissues
- Xenotransplantation Products
- Related Devices (including certain IVDs)

Response to Public Health Challenges

- CBER has responded to pandemic and emerging threats with proactive measures and focused efforts
  - Meetings to encourage/speed development of new products
  - Early and intensive ongoing interactions w/sponsors
  - Collaboration and rapid turnaround in product review
  - Inspections or site visits of manufacturing facilities
  - Increased communication with international regulatory counterparts
  - Critical Path Research: focused on priority areas to assist in more efficient, rapid product development and availability

Recent Vaccine Approvals

- 2008
  - Rotavirus Vaccine (Rotarix)
- 2007
  - H5N1 Influenza Vaccine
  - Smallpox Vaccine (ACAM2000)
  - Influenza Vaccine, trivalent, inactivated (Afluria)
  - Influenza Vaccine, trivalent, live (Flumist), extended indication down to age 2 yrs
  - Meningococcal conjugate vaccine (Menactra), extended indication down to age 2 yrs
- 2006
  - Rotavirus Vaccine (RotaTeq)
  - Herpes Zoster Vaccine (Zostavax)
  - Human Papillomavirus Vaccine (Gardasil)
  - Influenza Vaccine, trivalent, inactivated (FluLaval)

Major Vaccine Initiatives

- Pandemic influenza and emerging threat preparedness
- Enhancing product safety
  - Integrated safety teams and use of informatics
- Manufacturing and product quality activities
- Critical path
- Global collaboration

Pandemic Influenza: Meeting the Challenges

- Build review and testing capacity – including for surge and new vaccine technologies (e.g., adjuvanted, recombinant, or cell-culture grown vaccines)
- Influenza virus strain and reagent preparation needed for vaccine manufacture and testing
- Improved assays for evaluating vaccine potency, immune responses, etc.
- Support DHHS planning and vaccine development activities – enhance emergency vaccine availability preparedness

Pandemic Influenza: Meeting the Challenges (cont.)

- Pathways to speed development and availability
  - Guidances on clinical data needed to support licensure of seasonal and pandemic vaccines, including accelerated approval pathway (2007)
  - Draft Guidance on characterization and qualification of cell substrates used in production of viral vaccines (2006)
- Global outreach, cooperation, harmonization
- Licensure of H5N1 vaccine for persons 18-64 yrs of age at increased risk of exposure (2007)

Approaches to Speed Product Availability and Facilitate Licensure

- Early and frequent consultation between sponsor, end user (if different), and FDA.
- Availability for emergency use under IND or Emergency Use Authorization (EUA)
- Fast track (applies to development program)
- Priority review
- Accelerated approval
- Approval under “Animal Rule”
- Careful attention to risk/benefit and risk management issues

Accelerated Approval

- Product eligible if provides meaningful therapeutic benefit over existing treatments for serious or life-threatening illness
- Efficacy based on surrogate endpoint reasonably likely to predict clinical benefit
- Confirmatory post-marketing studies to verify clinical benefit
  - Usually underway at time of approval
  - Adequate and well controlled
- Withdrawal possible, e.g., if benefits not verified
- 3 new seasonal influenza vaccines received AA since 2005, doubling number of licensed influenza vaccines & increasing capacity for pandemic preparedness

Assuring Vaccine Safety

- Evaluate pre-licensure clinical, nonclinical, product, and manufacturing data, including facility inspection
- Pharmacovigilance plan evaluated as part of biologics license application and informs post-marketing surveillance and studies
- Lot release may be required prior to distribution of licensed products
- Biennial inspections
- Evaluation of post-marketing adverse event reports (VAERS) and studies

Enhancing Vaccine Safety

- Multi-disciplinary vaccine safety team (epidemiologists, clinical/product reviewers, compliance/manufacturing experts, communications) to improve acquisition, analysis, and communication of safety information
  - Encompasses entire product life cycle and all data relevant to safety, manufacturing, and compliance
  - Uses data to evaluate emerging safety issues
  - Coordinates FDA response to emerging safety issues with other HHS agencies (CDC, NVPO, NIH), industry
  - Enhances collaboration with other govt. agencies, WHO, and others on vaccine safety initiatives
  - Proactive: develop research, policy, outreach agenda

Collaboration with other Govt. Agencies on Vaccine Safety Monitoring

- CDC and Vaccine Safety Datalink
- PAHO/CDC/FDA post-marketing surveillance of rotavirus vaccines in Latin America
- Pilot project with CMS to evaluate safety of influenza and pneumococcal vaccines as part of pandemic preparedness
- MOU with Veterans Health Administration to share information on FDA-regulated products, including vaccines
- Collaboration with Department of Defense Medical Surveillance System and Vaccine Health Centers

Manufacturing and Product Quality Activities

- Enhance risk-based oversight and quality of manufacturing throughout product life cycle
- Continued training and outreach on vaccine quality and cGMPs
- Continued efforts to modernize and where possible to harmonize with other regulatory authorities (PIC/S)
- Risk-based compliance programs
  - Evaluate existing programs and expand to new areas

Manufacturing and Product Quality Activities (cont.)

- New CBER laboratories in newly created Division of Product Quality
  - Quality environment for critical product testing and standards activities
  - Ongoing efforts toward ISO certification
- Research to modernize approaches
  - Develop/evaluate more rapid potency and other lot release and product characterization assays
  - Enhanced methods to measure immune responses

CBER Critical Path: Bridge from Discovery to Products for Better Health

Biomedical Discovery

FDA/CBER

Products Improving Lives and our Nation's Health & Preparedness

- **Identify solutions to product development challenges: tools and pathways to cross bridge from discovery to real products**
- **Increased transparency and external input through Advisory Committees, Office Site Visits, FDA Science Board**
- **Research Management Leadership Council**

Critical Path and Vaccine Development

- Cell substrate safety and quality assays
- Collaborative efforts to develop/validate rapid sterility methods
- Adjuvants (NIAID interagency-agreement)
- Animal models for vaccine efficacy for BT agents and other emerging threats
- Improved influenza vaccine safety/quality assays
- Enhanced analytic tools for large databases and safety surveillance- in progress, including for influenza vaccines

Global Collaboration

- Leadership role of FDA, together with WHO and Health Canada, in Pandemic Influenza Vaccine Regulators Initiative
  - Develop convergence on data needed to evaluate pandemic influenza vaccines
  - Draft WHO Guidelines on Regulatory Preparedness for Human Pandemic Influenza Vaccines issued in 2007

Global Collaboration

- CBER is a WHO Collaborating Center
  - Expert Committee on Biologic Standards
  - Strategic Advisory Group of Experts
  - Global Advisory Committee on Vaccine Safety
  - Expert consultation in specific product areas (e.g., HIV, HPV, rotavirus, pneumococcal conjugate, influenza vaccines)
  - Participates in WHO teams to assess competency of national regulatory authorities (NRA) around the world
  - Training: Works with WHO Developing Countries Network to help build global regulatory capacity of NRAs to evaluate vaccine development and licensure

Global Collaboration

- International Conference on Harmonisation
- Pharmaceutical Inspection Cooperation/Scheme
- Information sharing agreements with other regulatory authorities (e.g., EMEA, Health Canada, and others) and engagement in priority areas (e.g., pandemic influenza vaccines) to facilitate global product development plans
- Partnering with WHO and NGOs to explore additional means of providing global regulatory assistance/capacity building

New Guidance

- Guidance for Industry: Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines (2007)
- Guidance for Industry: Clinical Data Needed to Support the Licensure of Trivalent Inactivated Influenza Vaccines (2007)
  - Provide guidance on clinical data needed to demonstrate safety and effectiveness for new influenza vaccines
  - Describe pathways for traditional and accelerated approval

Guidance (cont)

- Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (2007)
- Guidance for Industry: Considerations for Plasmid DNA Vaccines for Infectious Disease Indications (2007)
- Guidance for Industry: Considerations for Developmental Toxicity Studies for Preventive and Therapeutic Vaccines for Infectious Disease Indications (2006)
- Draft Guidance for Industry: Characterization and Qualification of Cell Substrates and Other Biological Starting Materials Used in the Production of Viral Vaccines for the Prevention and Treatment of Infectious Diseases (2006)

FDA Amendments Act (2007): Some Highlights

- **PREA: Pediatric studies required with application or supplement for new active ingredient, indication, dosage form, dosing regimen, or route of administration, unless deferral or waiver granted**
  - **Requires review division to consult with internal FDA review committee (PeRC) on pediatric plans, assessments, deferrals, waivers**
- **Priority review vouchers for products for tropical diseases: when application is approved, applicant receives a voucher that can be used for another products**
- **Safety: FDA to require post-marketing studies or clinical trials at time of approval, or after approval, based on certain safety concerns (e.g., signal of serious risk)**

FDA Amendments Act (cont)

- Safety Labeling Changes: certain changes trigger specific timelines for labeling negotiations and implementation
- Risk Evaluation and Mitigation Strategies: FDA can require at time of or after approval, based on safety information
- Active Post-market Risk Identification and Analysis System: to link and analyze safety data from multiple sources, with goal of including
  - at least 25M patients by 2010,
  - at least 100M patients by 2012

Summary

- FDA proactively facilitating development, licensure, and availability of new vaccines, including those
  - For pandemic and emerging threats
  - Manufactured using novel cell substrates, adjuvants, and recombinant technologies
- Developing needed pathways to speed development and enhance assessment of safety
  - New Guidance
  - New assays and standards to evaluate safety, potency, quality
  - Integrated vaccine safety team and close collaboration with CDC and other partners
- Global collaboration with WHO and others to encourage international convergence and more efficient product development through development of scientific and regulatory standards for safety, effectiveness, and product quality

Thank you!

- We are actively engaged in assuring the safety, effectiveness, and availability of products that touch so many lives and are critical for public health and preparedness
- Emerging threats, technologies, and opportunities demand constant renewal of scientific expertise and capacity
- The challenges and opportunities for leadership and public health are truly global – and collaboration is key!

CBER: INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

CBER Contact Information

www.fda.gov/cber

Manufacturers:

matt@cber.fda.gov

Consumers, health care professionals:

octma@cber.fda.gov

Phone: 301-827-1800