



FDA/CBER Activities to Advance Vaccine Development Programs Worldwide

Marion Gruber, PhD
Acting Director, Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
Food and Drug Administration

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Global Infectious Disease Vaccines

- The development of safe and effective vaccines to protect against global infectious diseases is of critical public health importance
 - Emerging and re-emerging disease
 - New vaccines of local and global importance
- Need for international engagement and collaborations and creative & flexible regulatory pathways to licensure

Global Collaboration: CBER

- Information sharing agreements with other regulatory authorities (e.g. EMA, HC)
 - Formation of international working groups, e.g. data needs to evaluate pandemic H1N1 2009 vaccine
- CBER is a WHO Collaborating Center
 - WHO developing countries network
 - Global Advisory Committee on Vaccine Safety
 - Strategic Advisory Group of Experts
 - Expert Committee on Biologic Standardization
- Assist developing Country NRAs, e.g., provide reviews, opinions, inspections, working with WHO/PAHO
- Training at NRAs on USFDA IND process including product review, and clinical protocol review

Collaborations with WHO

- Global Advisory Committee on Vaccine Safety
 - to enable WHO to respond promptly, efficiently, and with scientific rigor to vaccine safety issues
- Strategic Advisory Group of Experts (SAGE)
 - principal advisory group to WHO for vaccines and immunization
- Expert Committee on Biologic Standardization
 - to establish detailed recommendations and guidelines for the manufacturing, licensing, and control of blood products, cell regulators, vaccines and related in vitro diagnostic tests

WHO Developing Country Initiatives

African Vaccine Regulators Forum (AVAREF)

- Scientific advisory body including representatives from 19 African nations that helps define the oversight roles of NRAs of its member nations
- CBER provides guidance on regulating clinical trials of vaccines, interacting with national and local IRBs and ethical committees
- Goal of collaborations:
 - Strengthening NRA capacity to regulate new medical products
 - Increase the regulatory capabilities of NRAs in the African region.

WHO Developing Country Initiatives

- Developing Countries' Vaccine Regulators Network (DCVRN)
 - Network of national regulatory authorities from developing countries
 - Builds regulatory capacity among vaccine-producing countries through information-sharing, training, and organizing activities
 - FDA/CBER actively engages with the DCVRN to support the network's global regulatory capacity enhancement effort.

Role of CBER in Assisting NRAs

- Contributes to WHO training workshops to strengthen the regulatory capabilities of developing country NRAs, e.g.
 - Medical officer, CMC reviewers and other scientists from OVRP have served as advisers for a series of WHO training workshop aimed at strengthening the regulatory capabilities of the Thai FDA to perform independent evaluation of marketing authorization applications for vaccines
 - Training at NRAs on USFDA IND process including product review, and clinical protocol review
 - Provide reviews, opinions, inspections

WHO Reference Laboratory

- FDA is a part of the WHO Reference Laboratories Network
- FDA contributes to worldwide efforts to develop yearly influenza vaccines
 - Yearly seasonal influenza vaccine strain selection
 - Generation of reference virus strains and reference reagents for influenza vaccine production

CBER/Path Collaboration

MenAfriVac (meningococcal group A vaccine)

- OVRP researchers developed the conjugation technology for the development of a conjugate vaccine to prevent meningococcal meningitis in Africa
- Conjugation technology was used by the Meningitis Vaccine Project (MVP), a partnership between PATH and WHO, to make the vaccine
 - December 2009: MenAfriVac licensed by India
 - June 2010: WHO prequalified the vaccine.
 - Cost: 50 cents per dose
 - December 2010: MVP launched a vaccination campaign aimed at protecting millions of people in West Africa from meningococcal disease
- To date: ~ 20 million people have been immunized
- Protection of 450 million people; ~150,000 lives saved



CBER/Path Collaboration

- Collaboration with PATH regarding the MVP:
 - Example of how the FDA/CBER applies technologies it develops to public health issues in the United States and throughout the world.
 - Continuation the successful partnership between PATH and FDA/CBER
 - Evaluate the application of FDA/CBER's conjugation technology to pneumococcal vaccines.
 - Advance development of a vaccine to protect children against diseases caused by *Streptococcus pneumoniae* (pneumococcus)

WHO Vaccine Prequalification Program

- Under its vaccines prequalification program, WHO provides advice to United Nations purchasing agencies on the acceptability of vaccines considered for purchase by this agency.
- In FY 2009, CBER completed its first year as a reference NRA under the WHO vaccine prequalification program.
- CBER serves as the regulatory authority of record in the context of the WHO vaccine prequalification process.
- There are 8 vaccines on the list of WHO prequalified vaccines with CBER as reference NRA.
 - Including rotavirus vaccines, influenza vaccines and pneumococcal conjugate vaccines.

Providing flexible regulatory frameworks: Malaria TBV:

- Benefit of vaccination may accrue indirectly to the individual as a result of a decrease in the incidence and prevalence of the infectious agent in the community
 - Immune response may reduce disease transmission by vector
 - No direct protection to the individual but reduction in morbidity and mortality may be achieved over time
 - TBVs offer *no direct benefit* to the vaccinee
 - primarily conferring population benefit

Providing flexible regulatory frameworks: Malaria TBV: (cont.)

- Would the PHS Act and applicable regulations allow CBER to approve a biological product application for a malaria TBV ?
- No clear legal bar to approving a vaccine that confers no direct benefit on recipients
- Regulations governing biological product licensing do not on their face require that a biological product confer direct clinical benefit on recipients
- Designing clinical studies for such vaccine may raise ethical issues which need to be appropriately addressed in clinical development of such product

US Licensure Pathways for Global Infectious Diseases

- In 2008, FDA issued a guidance document on regulatory pathways for development of vaccines to protect against global infectious diseases for U.S. licensure.
- Guidance for industry document: General principles for the Development of Vaccines against Global Infectious Diseases (2008)
 - <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074762.htm>
- Focus on development of vaccines targeted against infectious diseases or conditions endemic in areas outside the US

Applicable Guidance (cont.)

- Provides general recommendations for regulatory pathways to use in the development of vaccines to protect against global infectious diseases for US licensure
- Clarifies regulations, statutes and guidance applicable to the development of these vaccines
- Clarifies several misconceptions surrounding the development of vaccines to protect against global infections in regard to US regulatory requirements

Applicable Guidance (cont.)

- FDA can license vaccines to protect against infectious diseases or conditions not endemic in the US
- The regulations are the same as for vaccines licensed for use in the US
- Clinical data from trials conducted outside the US can be used in support of US licensure
- Principles are supported by legislation (Food & Drug Administration Amendment Act [FDAAA] 2007, Addition of Section 524 to the FD&C Act)
 - Importance of having products to treat and prevent tropical diseases that disproportionately affect poor and marginalized populations and for which there is no significant market in developed nations

Applicable Guidance (cont.)

- FDA encourages sponsors to develop and license vaccines to protect against global infectious disease by submitting an IND (21 CFR part 312) including those situations where
 - The US market for that vaccine is limited
 - The primary target population for the vaccine is in developing countries

Applicable Guidance (cont.)

- This guidance was recently updated to reflect a shift in regulatory policy and current thinking:
- Demonstration of the effectiveness of a vaccine in a US population for a disease circulating in an endemic country may no longer be a requirement for licensure in every instance.



Thank you