CBER SAFETY INITIATIVES:
The Vaccine Safety Team

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Presentation Outline

- Vaccines: Brief Introduction
- Describe the Vaccine Safety Team (VST)
- Case Study: Hib vaccine recall because of lack of assurance of sterility

What is a Vaccine?

May contain all or a portion of the disease-causing or related organism or nucleic acid encoding one or more proteins from the organism.

- **Preventive vaccines**
- Intended to prevent infectious diseases by inducing a protective immune response
- **Therapeutic vaccines**
- Intended to treat infectious diseases or other diseases (e.g., cancer)

Challenges With Vaccines Manufacturing

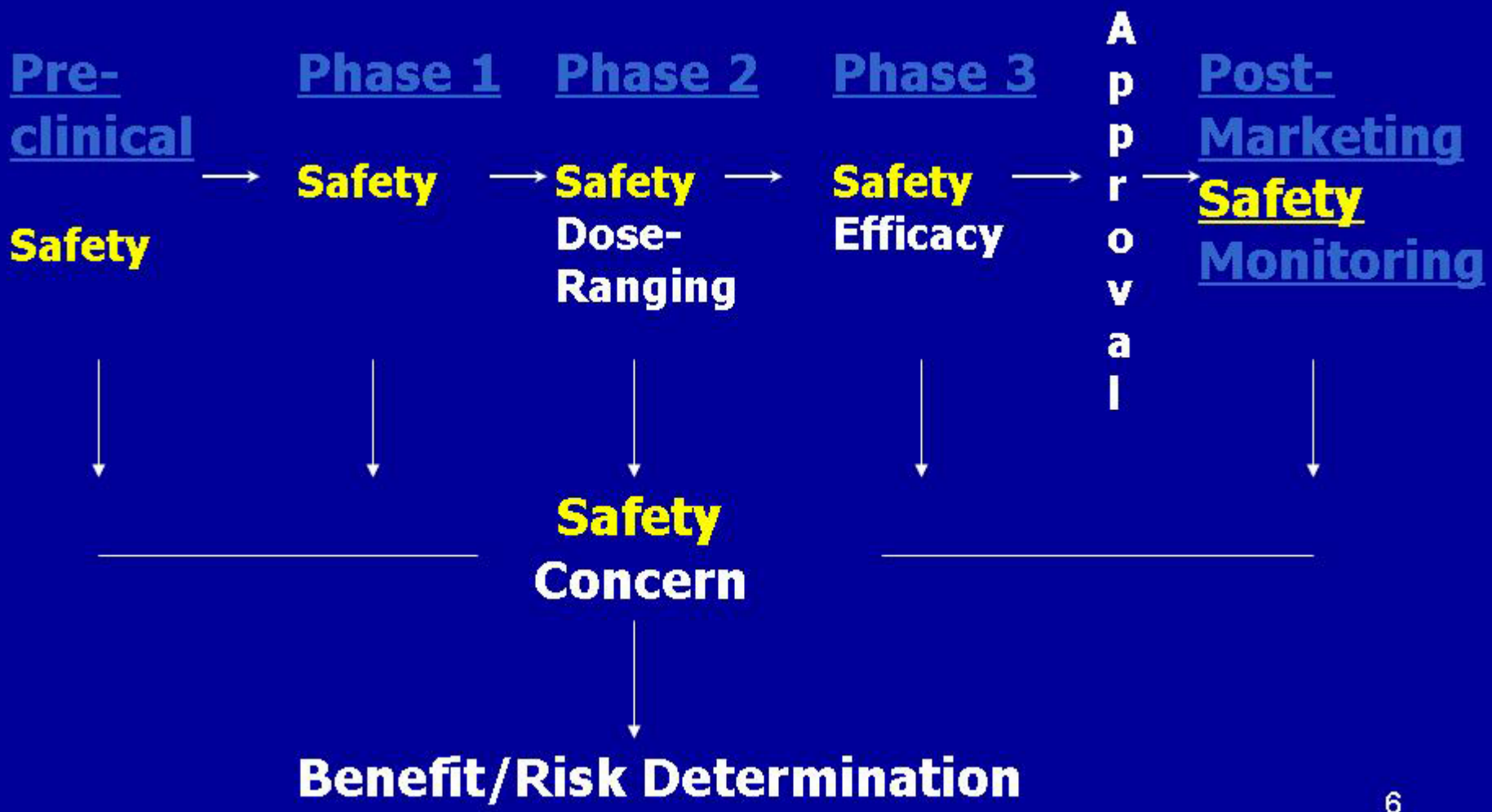
- Biologic sources of viral or bacterial seed, cell substrate, other components
  - Test for adventitious agents
  - For inactivated vaccines, validate inactivation process
  - For live vaccines, demonstrate attenuating characteristics retained
- Complex manufacturing processes: detailed procedures, testing, product characterization - critical for product consistency and quality
- Novel technologies and constituents

Challenges With Vaccines Safety Expectations

Vaccines are expected to be very safe

- **Childhood vaccination requirements**
  - ~ 4 million children per birth cohort per year
- **Expectations may change over time**
  - e.g., as risk of vaccine-preventable disease decreases
- **Public expectation**
  - Greater information on benefits/risks
- **New Technologies**
  - Are they safe? Are they providing benefits?
- **Global consequences**
  - e.g., RotaShield® and intussusception

Safety in the Lifecycle of a Vaccine



How can we enhance safety monitoring during the lifecycle of a vaccine?

Premarket Postmarket

Premarket ⟺ Postmarket

FDA Efforts to Enhance Vaccine Safety: Vaccine Safety Team

Mission

- CBER has formed the VST to:
- Provide rapid coordination, communication, and follow-up on safety issues involving complex intra-Center interactions
- Serve as a resource to the Center for identifying data and policy needs

What is the VST?

- Newly formed: first meeting held July 19, 2007 (monthly meetings)
- Multi-disciplinary vaccine safety team (epidemiologists, clinical/product reviewers, compliance/manufacturing experts, communications) to improve acquisition, analysis, and communication of safety information

Composition of the VST

- Members are from five CBER offices:
- Office of the Center Director (OD)
- Office of Biostatistics and Epidemiology (OBE) *
- Office of Communication, Training and Manufacturers Assistance (OCTMA)
- Office of Compliance and Biologics Quality (OCBQ)
- Office of Vaccines Research and Review (OVRR) *

* OBE/OVRR lead to integrate pre-and post-marketing

The VST

- Encompasses entire vaccine lifecycle and all data relevant to safety, manufacturing, compliance
- Uses data to evaluate emerging safety issues
- Coordinates FDA response to emerging safety issues with other HHS agencies (CDC, NVPO, NIH), industry, as needed
- Proactive: identifies data and develops policy needs
- Enhances collaboration with other government agencies, WHO, and others on vaccine safety initiatives

A Case Study:
Hib vaccine recall

A Case Study: Hib vaccine recall

- Hib vaccine prevents meningitis and other serious infections caused by a bacteria called *Haemophilus influenzae* type b
- It is recommended for all children under 5 years old in the U.S., and it is usually given to infants starting at two months old

Case Study (continuation)

- Dec. 12, 2007, Merck & Co., Inc. announced a voluntary recall of certain lots of the Hib conjugate vaccines, PedvaxHIB® (monovalent Hib vaccine) and COMVAX® (Hib/hepatitis B vaccine)
- During routine testing of the vaccine manufacturing equipment, Merck identified the presence of the bacteria *Bacillus cereus*
- *B. cereus* is a common cause of food poisoning. Non-GI *B. cereus* infections (e.g. wound healing, sepsis, meningoencephalitis, endocarditis, and pneumonia) can occur in immunocompromised persons

Case Study (continuation)

- Sterility tests conducted by Merck of the vaccine lots prior to release did not find any contamination in the vaccine
- However, because the company could not guarantee the sterility of certain specific lots of the vaccine, Merck conducted the recall
- The VST was alerted
- CDC and FDA conducted enhanced post-recall safety surveillance using VAERS, with emphasis on possible *B. cereus* infection in recipients of recalled vaccine.

Case Study (continuation)

- CDC used the Epidemic Information exchange (Epi-X) to contact public health departments asking for active surveillance of any *B. cereus* infections in vaccinated children
- No evidence of vaccine-associated *B. cereus* infection

Case Study (continuation)

What was the VST contribution to this safety emergency?

- The VST coordinated the necessary expertise (i.e., compliance/manufacturing, clinical, product, epidemiology) and center leadership to address this particular emergency
- Collaborated with CDC on an action on Hib vaccine shortage to recommend delaying the Hib vaccine booster dose for healthy children aged 12-15 months, except high-risk children

Summary

- The VST provides a multi-disciplinary and collaborative approach to coordinate:
  - emerging vaccine safety issues
  - emergency responses
  - communications
- Future challenges? New approaches, tools, current assumptions evaluation

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VST members:
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Thank you!