Regulatory Challenges of Licensing new Acellular Pertussis Vaccines

- DTaP vaccines contain one or more different Ags (e.g., PT, FHA, pertactin, fimbrial-2 and fimbrial-3 antigens all in different concentrations, and with different degrees of adsorption to different adjuvants.
- Individual antigens may be derived from different strains of *Bordetella pertussis,* with different methods of purification.
- Protective efficacy in humans of different vaccines may be based on different mechanisms
- No unequivocal immunological correlates of protection against pertussis have been demonstrated
- No generally accepted animal model to predict clinical efficacy has been validated

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- Safety and efficacy of a new formulations should be demonstrated in the target population,
- Difficult to undertake efficacy trials.
- Other criteria may be considered by regulatory authorities as predictors of clinical performance.
  - e.g., demonstrate the induction of immune responses equivalent to those induced by an approved homologous acellular pertussis vaccine of proven safety and efficacy
  - additional information about the physicochemical and immunological characteristics of any new vaccine formulation will be required to demonstrate equivalence with a homologous approved pertussis vaccine.

US FDA Considerations for Evaluation of Booster Doses of DTaP

- For DTaP vaccines already approved for a primary series, FDA has based decisions regarding approval of booster doses following a primary series of the same vaccine solely on safety data. In these instances, CBER has not required evaluation of the immune response to booster doses of DTaP vaccines.

What is the Issue?

- Waning immunity resulting in resurgence of pertussis disease
  - not a global resurgence
- Target population of morbidity and mortality
  - infants less than 3 months of age
- Options:
  - maternal immunization
  - newborn immunization

Summary

- Numerous immunogenicity and reactogenicity studies have been published evaluating acellular pertussis vaccines.
- Making comparison among currently licensed DTaP vaccines is difficult because of variations in previous study designs, study populations, and serologic assays.
- Difficult to do efficacy studies today.
- Licensure of new, more effective DTaP vaccines present regulatory as well as scientific challenges

Licensed Acellular Pertussis Vaccines in the US

- Tripedia
  - PT and FHA
- Infanrix (GSK)
  - PT, FHA, PRN
  - Combined with Hep B and IPV to form Pediarix
  - Combined with IPV to form Kinrix
- Daptacel (Sanofi)
  - PT, FHA, PRN, FIM-2 and FIM-3
  - Combined with IPV and Hib to form Pentacel
- Boostrix (GSK)
- Adacel (Sanofi)