Questions

Human Papillomavirus (HPV) Vaccines
Vaccines and Related Biological Products Advisory Committee Meeting
November 28-29, 2001
Bethesda, MD

1. **Please discuss and identify the most appropriate endpoints for traditional approval of HPV vaccines intended to prevent cervical cancer:**

   In particular, please discuss the use of the following endpoints in clinical trials intended to demonstrate the efficacy of HPV vaccines for oncogenic types, and the indications (e.g., prevention of HPV infection, etc.) these endpoints would support:

   a. Incident HPV infection by oncogenic HPV types (i.e., at least one positive HPV DNA test result).
   b. Persistent HPV infection by oncogenic HPV types.
      - ✓ Regarding this endpoint, please also discuss the appropriate number of positive virologic results, and the interval between positive virologic results.
   c. LSIL (cytology), associated with oncogenic HPV types.
   d. CIN 1, associated with oncogenic HPV types.
   e. CIN 2/3, associated with oncogenic HPV types.
   f. Cervical cancer.

2. **Please discuss the use of the accelerated approval regulations for licensure of HPV vaccines for the prevention of cervical cancer:**

   Specifically, please discuss and identify possible surrogate endpoints to support accelerated approval. In particular, consider the following endpoints:

   a. Incident HPV infection by oncogenic HPV types.
   b. Persistent HPV infection by oncogenic HPV types.
   c. LSIL (cytology), associated with oncogenic HPV types.
   d. CIN 1, associated with oncogenic HPV types.

   In the context of accelerated approval, please discuss and identify possible endpoints for the confirmatory trial.