Human Papillomavirus (HPV) Vaccine
Post-Licensure Monitoring and Implementation Activities
Centers for Disease Control and Prevention

1. Monitoring Disease Impact	Data anticipated	Lead CDC Center
Cancer		
Cancer Registries Cancer registration is the fundamental method in the United States by which information is systematically collected about the incidence and types of cancer. Surveillance for cervical cancer and other cancer incidence is currently done through CDC's National Program of Cancer Registries (NPCR) and National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) program. The combined NCPR and SEER data cover the entire United States. (http://seer.cancer.gov/) (http://www.cdc.gov/cancer/npcr/)	Trends in HPV-related cancers Combined NPCR and SEER data are provided in the *United States Cancer Statistics* series (http://apps.nccd.cdc.gov/uscs/)	NCCDPHP
HPV typing in Cervical and Non-cervical cancers Using data from registries supported by CDC's National Program of Cancer Registries, a pilot study has been initiated to identify cancer cases and to obtain paraffin block tissues for HPV genotyping to establish a pre-vaccine distribution (2004-2005) of HPV types in cervical cancer and non-cervical cancer cases in the four sites (Louisiana, Kentucky, Florida, and Michigan). Future periodic typing is planned.	HPV type distribution in cervical cancer HPV type distribution in vaginal, vulvar, anal, penile, and subset of oropharyngeal cancers.	NCCDPHP and NCZVED
CDC Monograph characterizing the epidemiology of HPV-associated cancers using National Program of Cancer Registries This monograph will use cancer registry data from the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology and End Results (SEER) program from 1998-2003. Using these years covers 83% of the U.S. population and allows for the examination of data prior to licensure of the HPV vaccine. The epidemiology of cancers that have been shown to be previously correlated with HPV will be characterized: cervix, vulva, vagina, penis, anus, and some oropharyngeal sites. (http://www.cdc.gov/cancer/npcr/)	Monograph in Journal *Cancer* in 2008	NCCDPHP
Cancer Precursors		
Cervical Intraepithelial Neoplasia (CIN) 2/3 monitoring in the Emerging Infections Program (EIP) Five EIP sites have been funded to develop and pilot an approach to monitoring HPV vaccine impact on cervical intraepithelial neoplasia (CIN) 2 and 3 diagnoses and associated HPV types. California, Connecticut, New York, Oregon and Tennessee will initially focus activities on well-	Population-based data on CIN2/3 including HPV type-specific incidence and detailed information on cases	NCHHSTP and NCZVED

characterized catchment areas ranging from 400,000 to 1.5 million in population with estimated 300-1800 CIN 2/3 cases annually. In addition to complete CIN 2/3 surveillance within the defined population, a randomly selected sample of CIN 2/3 cases will be investigated in more detail and HPV types will be determined. (http://www.cdc.gov/ncidod/osr/site/eip/index.htm)		
CIN3 monitoring in the National Program of Cancer Registries (NPCR) Three central (state-based) NPCR registries will be funded to pilot an approach to registration and collation of data on cervical precancers (cervical intraepithelial neoplasia (CIN) 3). Demographic data to be collected along with case information include age, race, county-level data. Attempts will be made to link the data from cancer registries to other morbidity and mortality data such as state based immunization registries to obtain HPV vaccination information. (http://www.cdc.gov/cancer/npcr/)	Broad state-based data on CIN 3	NCHHSTP and NCCDPHP
HPV outcomes monitoring in the Vaccine Safety Datalink (VSD) The project will describe the incidence and prevalence of HPV-associated conditions and outcomes in 3 VSD sites, (including genital warts, vulvar and vaginal lesions, and abnormal cervical cytology). This evaluation will be conducted as a baseline assessment (years 2000-2005) and a follow-up assessment after vaccine introduction. (http://www.cdc.gov/od/science/iso/research_activties/vsdp.htm)	Managed Care Organization based data on HPV related outcomes	NCHHSTP and NCZVED
Administrative datasets CDC will be working with with Thomson's Medstat Marketscan dataset to evaluate claims data on a large claims dataset including claims from 150 insurers. The Medstat population is representative of the insured population of the US and data on HPV vaccination rates, HPV associated cervical lesions, genital warts and health care utilization costs will be collected to monitor impact of HPV.	Administrative data on HPV-related diagnoses and procedures. Cost data associated with HPV related outcomes	NCHHSTP
Monitoring impact of HPV vaccine in Alaska The Arctic Investigations Program (AIP) at CDC is working on several HPV vaccine- related projects in Alaska, including 1) evaluating the impact of HPV vaccine on cervical cytology; 2) conducting long term HPV genotype surveillance among women attending colposcopy clinics in Anchorage, Alaska, and; 3) conducting HPV genotyping of cervical cancer specimens from Alaska. (http://www.cdc.gov/ncidod/aip/)	Trends in type-specific CIN lesions and cancer in the Alaskan native population	NCHHSTP and NCZVED
Genital Warts		
Wart monitoring in the STD Surveillance Network (SSuN) The SSuN is a network of 40 STD clinics in 12 geographic areas in the U.S. collaborating to monitor trends in STDs and related behaviors.. STD clinic data will be used to assess the prevalence and incidence of genital warts, treatment information, and HPV vaccine history. Changes in the healthcare utilization for genital warts related care will also be monitored.	Prevalence and incidence of genital wart diagnoses in the STD population.	NCHHSTP
Genital warts monitoring through the Vaccine Safety Datalink (VSD) CDC, in collaboration with VSD sites, will evaluate HPV associated conditions, including genital warts. This evaluation will be conducted as a baseline assessment (years 2000-2005) and a follow-up assessment after vaccine introduction. The outcomes to be evaluated include genital warts. A chart review will be done to validate administrative codes for these diagnoses.	Prevalence of warts and chart validation of ICD-9 code, utilization of STD clinic services for genital warts	NCHHSTP and NCZVED

(http://www.cdc.gov/od/science/iso/research_activties/vsdp.htm)		
Administrative datasets (see above)	Prevalence of wart diagnoses and associated procedures	NCHHSTP
HPV Type specific prevalence		
National Health and Nutrition Examination Survey (NHANES) NHANES is a national survey that collects data on the health and nutritional status of the US population. HPV DNA prevalence in self -collected vaginal swabs in women 14-59 years of age began in 2002. Continued monitoring through NHANES on a periodic basis could provide data on prevalence in a representative sample of the U.S. population. Sera are being tested for antibody to HPV types 6, 11, 16 and 18. (http://www.cdc.gov/nchs/nhanes.htm)	Type specific HPV prevalence among a random sample of women in the US Prevaccine era seroprevalence of HPV types 6, 11,16 ,18	NCHHSTP, NCZVED, and NCHS
HPV outcomes monitoring in the Vaccine Safety Datalink (VSD) The VSD project will determine the distribution of HPV types in cervical specimens and CIN 2/3 lesions collected from girls and women ages 11 to 29 years prior to HPV vaccine uptake. A future study will evaluate potential changes in types after vaccine introduction. Two VSD sites are participating: Northwest Kaiser Permanente and Northern California Kaiser Permanente. (http://www.cdc.gov/od/science/iso/research_activties/vsdp.htm)	HPV type specific data on CIN 2/3 and Pap specimens	NCHHSTP
Baseline collection of biopsy samples from North Carolina A pilot project to evaluate feasibility of specimen collection and testing is being conducted in North Carolina. Stored cervical biopsies will be obtained from the following disease categories: invasive cervical carcinomas, CIN 3 (severe dysplasia) and CIN 2 (moderate dysplasia). Type-specific prevalence of HPV will be calculated in each stage of cervical biopsies collected.	Pre-vaccine HPV type distribution in CIN and invasive cancers in North Carolina and feasibility of specimen collection and typing	NCHHSTP and NCZVED
Pilot study of HPV DNA testing in cervical cancer screening programs (see Behavior and Health Care)	Pap and HPV results for 8000 women in study Type specific HPV prevalence for underserved women	NCCDPHP and NCZVED
2. Monitoring Vaccine Coverage	**Data anticipated**	
National immunization Survey (NIS) NIS is a national survey that monitors childhood and adolescent immunization coverage for children and teens in the U.S. population and is a random-digit dial telephone survey. The NIS will be used to obtain nationally representative estimates of HPV coverage among adolescents 13 to 17 years of age, including provider verification of vaccination status. The adolescent module was added in the 4th quarter of 2006 and 2007. State specific data will be collected in 2008. An adult module was added to the NIS in summer of 2007 without provider verification of immunization status. (http://www.cdc.gov/nis/)	Vaccine coverage, knowledge of HPV and HPV vaccine, likelihood of receiving vaccine among those who have not received it	NCIRD
National Survey of Children's Health (NSCH) The NSCH provides both national and state based estimates. The survey was first done in 2003 and will be repeated in 2007. The survey involves a national sample of about 90,000 children - including about 2000 per state. This telephone survey includes interviews of approximately	Vaccine coverage	NCIRD

20,000 households with 12 to 17 year olds. Questions in 2007 include those related to HPV, and other adolescent vaccines. Immunization data will be based on parental recall. (http://www.cdc.gov/nchs/about/major/slaits/nsch.htm)		
National Health Interview Survey (NHIS) NHIS is a national survey used to monitor the health of the U.S. population. It provides national estimates on an annual basis. Estimates can also be made for the most populous states. The NHIS is a household survey. Questions were added to the 2008 NHIS on HPV vaccine receipt for adults 18 to 64 years of age and for children 8 to 17 years of age. (http://www.cdc.gov/nchs/nhis.htm)	Vaccine coverage	NCIRD
Behavioral Risk Factor Surveillance System (BRFSS) BRFSS provides national and state based estimates on an annual basis. The BRFSS is a random-digit-dial telephone survey. Questions on HPV vaccine coverage will be a module on the 2008 survey, but it is unknown which states will administer the questions. Questions will be asked to female adults 18 to 49 years of age and to parents of female children 9 to 17 years of age. (http://www.cdc.gov/brfss/)	Vaccine coverage	NCIRD
Immunization Information System Sentinel Sites (IISSS) Immunization Information Systems (IIS), previously known as immunization registries, are confidential, population-based information systems capable of activities that include collecting vaccination data from multiple health-care providers and assessing vaccination coverage in a defined geographic area. IIS have historically focused on children <6 years. IIS Sentinel Sites (IISSS) receive additional grant funding to allow achievement of higher data quality, and routine analysis of data to inform program operations. The IISSS for 2008-2012 are currently comprised of eight sites. Since its launch in the 3rd quarter of 2006, an Adolescent Module has been used by sites to collect coverage estimates for vaccines recommended for persons aged 11-18 years. (http://www.cdc.gov/vaccines/programs/iis/activities/sentinel-sites.htm)	Vaccine coverage	NCIRD
National Health and Nutrition Examination Survey (NHANES) **The National Survey of Family Growth (NSFG)** **Vaccine Safety Datalink (VSD)** Information on vaccine coverage will also be available from these surveys and studies (see other sections)	Vaccine coverage	NCIRD, NCHHSTP ISO
3. Behavior and Health Care	**Data anticipated**	
The National Survey of Family Growth (NSFG) NSFG is a national survey of approximately 4400 15 to 44-year-old women that provides current information on fertility and family planning. This nationally-representative data set includes detailed questions on sexual risk and STDs. Questions have been added to the current NSFG interviews that in conjunction with existing questions already asked by NSFG offer an opportunity to gauge changes in sexual risk and sexual health care seeking that may accompany an HPV vaccine. Questions are asked of women age 15-25 and mothers of daughters age 9-18. Also, the NSFG asks separate questions about pelvic exam and Pap test during the past 12 months. (http://www.cdc.gov/nchs/nsfg.htm)	Awareness of HPV, vaccine status, intention to get vaccinated, sexual behavior, and trends in cervical cancer screening.	NCHHSTP

Healthy Passages Healthy Passages is a community-based longitudinal survey of adolescent health, which will include questions for parents on the HPV vaccine. Additional questions have been added to wave II asking parents questions about their 5th and 6th grade child's (girls) vaccine status and likelihood of getting vaccinated in the next year. (http://www.cdc.gov/HealthyYouth/HealthyPassages/)	Cohort analysis of HPV vaccine status and sexual behaviors	NCCDPHP and NCHHSTP
Behavioral Risk Factor Surveillance System Cancer Control Supplement (BRFSS) BRFSS provides national and state based estimates on an annual basis. The BRFSS is a random-digit-dial telephone survey. Questions for women regarding cervical cancer screening and Pap tests are included in this survey. (http://www.cdc.gov/brfss/)	Trends in cervical cancer screening	NCCDPHP
National Health Interview Survey Cancer Control Supplement (NHIS) NHIS is a national survey used to monitor the health of the U.S. population. NHIS provides national estimates on an annual basis. Estimates can also be made for the most populous states. The NHIS is a household survey. Questions for women regarding cervical cancer screening and Pap tests are included in this supplement to the core survey. Http://www.cdc.gov/pub/Health_Statistics/NCHS/Survey_Questionnaires/NHIS/2005/English/QCANCER.pdf	Trends in cervical cancer screening	NCCDPHP
Pilot Study of HPV DNA testing in cervical cancer screening programs During this pilot study, HPV DNA testing as part of cervical cancer screening will be introduced and reimbursed to all providers within selected clinics (urban and rural sites) in the Illinois Breast and Cervical Cancer Early Detection Program (BCCEDP) for providers to use for their patients 35 years of age and older. HPV (HC2 and Genotyping) and Pap test results will be available for 8000 women in the study.	Provider practices in cervical cancer screening	NCCDPHP and NCZVED
EDRN-CDC Biorepository for Biomarker Studies of Cervical Cancer (EDRN CDC IAA) The biorepository is part of NCI's Early Detection Research Network (EDRN), funded through an Interagency Agreement with CDC. Biospecimens (cervical cells, cervical mucous, serum, plasma and WBCs) are collected from consenting women at the time of colposcopy and at intervals for 2 years. Samples are linked to HPV status, cervical disease and epidemiologic data. Promising biomarkers are evaluated in the context of these data to evaluate those that identify the minority of women who need treatment. (http://edrn.nci.nih.gov/)	Biomarkers to improve efficiency of cervical cancer screening	NCZVED
4. Monitoring Vaccine Safety	**Data anticipated**	
Vaccine Adverse Event Reporting System (VAERS). VAERS is a passive reporting system that is used as an early warning system for vaccine safety. This project is one of the cornerstones of post-licensure safety surveillance and is a national spontaneous reporting system jointly operated by CDC and FDA. Although VAERS has well described limitations including underreporting and inability to determine causal relationship to vaccination for most reports, it can allow hypothesis generation. (http://vaers.hhs.gov/)	Adverse events reported in relation to HPV vaccine	ISO
Vaccine Safety Datalink (VSD) VSD is a collaborative project between CDC and a group of managed care organizations (MCOs) that investigate possible vaccine-related events through systematic studies and evaluations of data	Adverse events related to HPV vaccine	ISO

collected in the MCOs. VSD includes the Rapid Cycle Project Analysis which specifically looks at outcomes of concern for early evaluation. (http://www.cdc.gov/od/science/iso/research_activties/vsdp.htm)		
5. Vaccine implementation		
HPV Vaccination in Communities with High Rates of Cervical Cancer This project is being conducted in 5 rural counties in North Carolina and in Los Angeles County. The goals are to evaluate parent and provider knowledge and attitudes about HPV vaccine, identify obstacles and opportunities for vaccine delivery to community adolescents, assess HPV vaccine uptake and predictors of vaccination, and develop a community plan for enhancing HPV vaccine delivery.	Parent and provider attitudes and intentions to vaccinate, predictors of vaccination in high-risk communities	NCHHSTP
Rochester Center for Adolescent Immunization Research (RCAIR): provider survey This is a national survey of ~800 Pediatricians and ~1100 Family Physicians about adolescent immunization. HPV specific questions on implementation of recommendations, barriers to vaccination, and concerns over duration of immunity will be included.	Provider attitudes and barriers to vaccination	NCIRD
Rochester Center for Adolescent Immunization Research (RCAIR): parent and teen survey This survey of ~360 parents and ~300 adolescents (15 to 17 years of age) who attend pediatric practices in Monroe County, NY will assess knowledge, attitudes, and beliefs related to adolescent vaccines. HPV specific questions include knowledge of HPV disease/vaccine, reasons for/against vaccination, appropriate ages to begin STI discussions with teen, and beliefs about HPV vaccine changing teen's sexual behavior.	Parent and teen knowledge, attitudes, and beliefs	NCIRD
Feasibility of delivering new adolescent vaccines in complementary healthcare settings This project will evaluate the feasibility of delivering adolescent vaccines, including HPV, in complementary healthcare settings. Key informant interviews will be conducted in each setting to determine feasibility of providing vaccines. Surveys of parents and adolescents will be conducted to determine the acceptability and likelihood of receiving vaccines in these settings.	Feasibility/likelihood of providing vaccine in alternate settings	NCIRD
Adolescent reminder/recall A randomized control trial will be conducted to evaluate the effectiveness of reminder/recall activities to increase vaccination coverage among adolescents. Reminders include notices to parents of adolescents who are coming due for a vaccination; recall includes notices to parents of adolescents who are overdue for a vaccination. Activities will be conducted in public/private, urban/rural, and pediatric/family medicine settings.	Effectiveness of reminder/recall strategy to increase completion of adolescent vaccinations, including the HPV series	NCIRD
Adolescent consent laws The Center for Adolescent Health and the Law has written a monograph describing the laws around adolescent consent for STD care. This project will append to this monograph the laws and interpretation of statutes in all 50 states concerning adolescent consent for immunization	Laws and interpretation thereof for adolescent consent for vaccination	NCHHSTP and NCIRD
School based vaccination project Schools have been looked to as a potential location for accessing and vaccinating large numbers of adolescents. This demonstration project, conducted in several middle schools in Denver, CO, will assist CDC evaluate the feasibility of conducting school based adolescent vaccination activities and the ability to bill health insurance plans for reimbursement of vaccination services for insured students.	Proportion of middle school students receiving recommended vaccinations (including HPV) and cost to implement	NCIRD

Provider Survey for HPV vaccine Researchers from the University of Colorado will administer a nationwide survey to ~400 Pediatricians and ~400 Family Physicians to assess implementation of quadrivalent HPV vaccine, barriers to vaccination, and preference for quadrivalent vs. bivalent vaccine.	Provider attitudes and barriers to vaccination	NCIRD
6. Vaccine related research	**Data anticipated**	
Immunogenicity and duration of antibody in Alaskan Natives The Artic Investigations Program (AIP) at CDC has a long history of vaccine evaluation. CDC has initiated several studies to evaluate HPV vaccine in the Alaskan Natives. This study will evaluate the immunogenicity and duration of the immune response after HPV vaccine among a population of adolescent Alaskan Natives. (http://www.cdc.gov/ncidod/aip/)	Immunogenicity and duration of antibody response among Alaskan natives	NCHHSTP
7. Communications and education	**Data anticipated**	
HPV communications research with special populations This study included focus groups to test messages and designs targeting 18-29 year-old Vietnamese, Korean, Filipino and American Indian/Alaskan Native men and women for use in educational posters and brochures.	HPV & cervical cancer awareness/knowledge, information sources, and communication needs, and preferences. Data collected in Feb-March 2007	NCHHSTP
Media and public engagement campaign targeting parents and caregivers of Native American and Asian pre-teens This study will conduct focus groups to explore Korean, Vietnamese, and Native American caregivers' knowledge, attitudes, and beliefs about preteen vaccination and the HPV vaccine. The study will also test educational materials and motivational messages about the HPV vaccine. Findings will be used to develop educational messages and materials for both communities.	Qualitative knowledge, attitudes, and behaviors data on the three pre-teen vaccines, including HPV vaccine, information about messages and dissemination	NCIRD and NCHHSTP
Pre-teen vaccine campaign CDC has created a media and public information campaign to educate Caucasian, African American and Hispanic parents of 11 and 12 year olds and the healthcare providers who serve them about the three pre-teen vaccines (including HPV vaccine) and the 11 and 12-year-old medical check-up. As new components of the campaign are designed, they will be tested with the target audience.	Qualitative knowledge, attitudes, and behaviors data on the three pre-teen vaccines, including the HPV vaccine; information about messages	NCIRD
8. Modeling	**Data anticipated**	
Harvard modeling team CDC is working with this team who has developed transmission models and Markov models to examine a range of issues. Key projects will include comparing the cost-effectiveness of the two HPV vaccines and examining cost-effectiveness of HPV vaccination by age.	Model-based estimates of impact and cost-effectiveness of vaccination	NCHHSTP
CDC modeling CDC modeling efforts include continued development of an alternative model based on observed incidence of HPV-related health outcomes (cervical and other cancers, CIN1-3, and genital warts). Key projects will include comparing the cost-effectiveness of the two HPV vaccines and examining cost-effectiveness of HPV vaccination by age.	Model-based estimates of impact and cost-effectiveness of vaccination	NCHHSTP

Conjoint Analysis Conjoint analysis can be used to elicit preferences about vaccine attributes. A study is being planned to evaluate HPV vaccine as a "test case" for possible future application to other vaccines.	Preferences and relative importance (valuation) of different features/attributes of HPV vaccines (e.g., value of protection against warts)	NCIRD

Lead CDC Center Key:
NCIRD: National Center for Immunizations and Respiratory Diseases
NCHHSTP: National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
NCCDPHP: National Center for Chronic Disease Prevention and Health Promotion
NCZVED: National Center for Zoonotic, Vector-Borne, and Enteric Disease
NCHS: National Center for Health Statistics
ISO: Immunization Safety Office