Oregon Immunization School/Facility/College Law Advisory Committee:

Review of Human Papillomavirus (HPV) Against Twelve Criteria for School/Facility/College Immunization Requirements

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Process for Reviewing Antigens for Potential Inclusion in OAR 333-050-0050, 333-050-0130 and 333-050-0140.

Request for the inclusion of additional antigens or vaccines can come from the Oregon Immunization Program, IPAT (Immunization Policy Advisory Team), or from the community. Proposed changes to vaccine requirements are discussed with IPAT either in a regularly scheduled meeting or through electronic communication. IPAT will submit their comments and a request for consideration to the Oregon Immunization School Law Advisory Committee.

The Oregon School/Facility Immunization Advisory Committee was established as a part of the school law immunization requirements when the original legislation was passed in 1980. This Committee is composed of immunization stakeholders from the fields of public health, school health, school administration, medicine, day care, child advocacy and consumers (parents). Through consensus, the committee determines what vaccines (antigens) should be included in Oregon school immunization requirements.

Information about new vaccines and the disease they prevent, including transmission within schools, burden of disease, cost-effectiveness, affect on schools/counties and vaccine availability is presented at a scheduled meeting for committee consideration. The following criteria are an integral part of the discussion and the decision-making process. All 12 criteria must be considered. Members of the Committee are expected to rely on their professional and scientific judgment as well as available data when applying the criteria.

The Committee's recommendation is then submitted to the Oregon Immunization Program for consideration and possible action.

The decision was made by the School/Facility/College Immunization Law Advisory Committee to recommend not requiring HPV vaccine for school attendance in Oregon on December 9, 2009.

The 12 Criteria to Consider in Evaluating HPV

The following information is being presented for Committee consideration. ACIP has recently made a provisional recommendation that HPV vaccine may be given to males. The impacts of adding males are in boxed text related to each of the criteria.

1. **The vaccine containing this antigen is recommended by ACIP (Advisory Committee on Immunization Practices) and included on its recommended childhood and adolescent immunization schedule**.

   From:
   CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 11th Edition, pages 123-133. [1]

   > "Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States… Epidemiologic studies showing a consistent association between HPV and cervical cancer were published in the 1990s. The first vaccine to prevent infection with four types of HPV was licensed in 2006… HPV is transmitted by direct contact, usually sexual, with an infected person. Transmission occurs most frequently with sexual intercourse but can occur following non-penetrative sexual activity… Non sexual routes of genital HPV transmission include transmission from a woman to a newborn infant at the time of birth."

   ACIP recommends that the HPV vaccine be administered to all adolescent girls and women 11 – 26 years of age, and the vaccine can be given as young as 9 years of age. The series consists of three doses given over a period of six months. A quadrivalent vaccine (Gardasil®) was licensed in 2006. A bivalent vaccine (Cervarix®) was licensed in 2009, and ACIP recommendations will be published in the future for this vaccine.

   In October 2009, ACIP issued this statement regarding HPV for males: "The 3-dose series of quadrivalent HPV vaccine may be given to males aged 9 through 26 years to reduce their likelihood of acquiring genital warts. Ideally, vaccine should be administered before potential exposure to HPV through sexual contact." [2]

2. **The vaccine prevents disease with a significant morbidity and mortality in at least some subset of the Oregon's population.**

   In Oregon, there are approximately 23,000 abnormal pap smears, 120 new cases of cervical cancer and 40 deaths from cervical cancer annually.[3]

   FDA approved the use of the quadrivalent HPV vaccine Gardasil® in males only for the prevention of genital warts. The vaccine may have benefits in terms of prevention of anogenital cancers in males and females, though these benefits are likely to be substantially lower than those seen with vaccination of females.

3. **The vaccine (antigen) is cost-effective from a societal perspective in Oregon.**

From:
Kim and Goldie. Health and Economic Implications of HPV Vaccination in the United States. *N Engl J Med*. 2008 Aug 21;359(8):821-32.[4]

> "On the assumption that the vaccine provided lifelong immunity, the cost-effectiveness ratio of vaccination of 12-year-old girls was $43,600 per quality-adjusted life-year (QALY) gained, as compared with the current screening practice. Under baseline assumptions, the cost-effectiveness ratio for extending a temporary catch-up program for girls to 18 years of age was $97,300 per QALY… The results were sensitive to the duration of vaccine-induced immunity; if immunity waned after 10 years, the cost of vaccination of preadolescent girls exceeded $140,000 per QALY, and catch-up strategies were less cost-effective than screening alone. The cost-effectiveness ratios for vaccination strategies were more favorable if the benefits of averting other health conditions were included or if screening was delayed and performed at less frequent intervals and with more sensitive tests; they were less favorable if vaccinated girls were preferentially screened more frequently in adulthood."

> "The cost-effectiveness of HPV vaccination will depend on the duration of vaccine immunity and will be optimized by achieving high coverage in preadolescent girls, targeting initial catch-up efforts to women up to 18 or 21 years of age, and revising screening policies."

> "When the potential benefits associated with preventing noncervical HPV-16–related and HPV-18–related cancers and HPV-6–related and HPV-11–related juvenile-onset recurrent respiratory papillomatosis were included, cost-effectiveness ratios were reduced. The magnitude of these reductions depended on the specific outcomes that were included and on assumptions about the efficacy of the vaccine. In all scenarios, the cost of vaccination of preadolescent girls remained below $50,000 per QALY, and catch-up vaccination of girls to 18 years of age remained between $50,000 and $100,000 per QALY."

From:
Kim and Goldie. Cost effectiveness analysis of including boys in a human papillomavirus vaccination programme in the United States. *BMJ*. 2009 Oct 8;339:b3884.[5]

"With 75% vaccination coverage and an assumption of complete, lifelong vaccine efficacy, routine HPV vaccination of 12 year old girls was consistently less than $50 000 per QALY gained compared with screening alone. Including preadolescent boys in a routine vaccination programme for preadolescent girls resulted in higher costs and benefits and generally had cost effectiveness ratios that exceeded $100 000 per QALY across a range of HPV related outcomes, scenarios for cervical cancer screening, and assumptions of vaccine efficacy and duration. Vaccinating both girls and boys fell below a willingness to pay threshold of $100 000 per QALY only under scenarios of high, lifelong vaccine efficacy against all HPV related diseases (including other non-cervical cancers and genital warts), or scenarios of lower efficacy with lower coverage or lower vaccine costs."

HPV vaccine is expensive, various models of cost-effectiveness give different estimates, and it is not clear that its use in males will be cost-effective.

4. **The vaccine (antigen) has been used in the general population to demonstrate reduction in disease activity with similar level of effectiveness to that demonstrated prior to FDA approval.**

From the Vaccine Information Statement for HPV:[6]

"Several mild problems may occur with HPV vaccine:

- Pain at the injection site (about 8 people in 10)
- Redness or swelling at the injection site (about 1 person in 4)
- Mild fever (100°F) (about 1 person in 10)
- Itching at the injection site (about 1 person in 30)
- Moderate fever (102°F) (about 1 person in 65)"

Syncope or fainting has also been reported. It is suggested that patients wait 15-20 minutes after receiving the vaccine before leaving.[1]

It is difficult to demonstrate a reduction in disease outcomes as potential cases of cervical cancer may not appear until many years later.

The vaccine has not been used in males in the general community, so there are no data on side-effects or reduction in disease related to such use.

5. **The vaccine is necessary to prevent diseases known to be spread in schools or facilities, respectively and will increase safety in the school/facility environment.**

HPV vaccine does not prevent a disease that is readily spread in school settings.

6. **Requiring the vaccine for school law will make a significant difference in vaccine coverage in the preschool/school/college populations and vaccinating the infant, child, adolescent or young adult against this disease reduces the risk of person-to-person transmission.**

"Herd protection" cannot be achieved if only females are vaccinated. Vaccinating females provides some protection because the virus has less opportunity to spread within the community, but risk factors related to sexual behavior including number of sex partners, lifetime history of sex partners, and the partners' sexual histories affect the outcomes and potential for infection. Consideration should be given as to how the disease is transmitted and whether disease will spread in the school, preschool or college environment.

It is reasonable to presume that by adding HPV vaccination to requirements for school attendance, HPV coverage will increase; its effect on disease transmission is not known, because vaccination rates among girls and women have not yet stabilized.

7. **The vaccine is acceptable to the Oregon medical community and the general public.**

Data for adolescent females from quarter two of 2009 Oregon Sentinel Region indicate that 20.3% of 11 – 12 year olds, 36.7% of 13 – 15 year olds, and 38.7% of 16 – 18 year olds have received 1 or more doses of HPV. For three doses of vaccine, the percentages are as follows: 5.9% of 11 – 12 year olds, 15.6% of 13 – 15 year olds, and 17.8% of 16 – 18 year olds.[7]

We have no history or information as to what the uptake might be regarding males receiving this vaccine. It is likely to be low, given ACIP's "may be given" statement and "permissive" VFC authorization; and the lower incidence of serious HPV-related disease in males, compared to those in females. For similar reasons, more resistance to a school requirement for use of this vaccine in males is likely.

8. **Ensure that sufficient funding is available on a state level to purchase vaccines for children who would need to meet the new law requirements.**

Estimates for funding requirements were based on several factors, including the ACIP recommendations of three doses of HPV for every female from 11 – 18 years of age, the assumption that the vaccine requirement would be phased in over several years, and the percentage of adolescents covered by different vaccine funding sources. It is estimated that a requirement for HPV vaccine would cost the state general fund $455,829 during the first year and $700,564 during the second year, for a total of $1,156,393 for the first biennium of this requirement.[8]

Using the assumption that insurance coverage and funding sources for the vaccine are the same for males and females, the cost would double for a total of $2,312,786 for the biennium. However, the permissive recommendation allows VFC providers to choose not to stock or recommend HPV vaccine for males, and insurance may not cover this vaccine for males, so the cost to the state general fund could be over $12,000,000 for the first biennium.

9. **There is a stable and adequate supply of vaccine.**

There appears to be a sufficient supply of vaccine for females at the current time especially with the recent addition of another HPV vaccine.

Only Gardasil® is currently approved for use in males, and vaccine supply for this group is unknown.

10. **The administrative burdens of delivery and tracking of vaccine and Oregon school/facility rule implementation is reasonable in light of any other vaccines currently being phased in to law.**

There would be significant financial costs in adding a new vaccine to the school law requirements. Projected costs are from $100,000 – 150,000 for programming to track the vaccine and revise exclusion orders in the systems. Approximately 90% of children attending public schools are tracked through school-based computer assessment systems. These computer assessment systems must submit test cases and have their programs approved by the state. Applying a required immunization to only one gender would require additional computer programming changes and incur additional costs.

The phase-in of the Tdap and Hepatitis A requirements is scheduled to continue until school year 2014-2015. Implementing overlapping phase-in schedules at the same time is difficult. The Advisory Committee previously affirmed their position to not add immunization requirements during the phase-in of other requirements, although consideration could be made in special circumstances such as increased disease incidence.[9]

Using the same recommendation for males and females would eliminate the need for school-based computer assessment programs to track HPV vaccine based on gender.

11. **The burden of compliance for the vaccine is reasonable for the parent/caregiver.**

Parents are already taking students in for the Tdap vaccine, but HPV is a three-dose series that would triple the number of appointments parents would be required to make.

The burden is substantial: the addition of this vaccine would necessitate two additional visits for adolescent males.

12. **The vaccine is included in Oregon ALERT IIS for tracking and reporting purposes.**

The vaccine is included in ALERT for tracking and reporting purposes.

References:

1. Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hpv.pdf
2. Available at: http://www.cdc.gov/vaccines/recs/provisional/downloads/hpv-vac-dec2009-508.pdf
3. Available at: http://www.oregon.gov/DHS/ph/imm/docs/HPVGuideintro.pdf
4. Available at: http://content.nejm.org/cgi/content/full/359/8/821
5. Available at: http://www.bmj.com/cgi/reprint/339/oct08_2/b3884
6. Available at: http://www.cdc.gov/vaccines/pubs/vis/downloads/vis-hpv.pdf
7. Sentinel region data—The sentinel region consists of 42 zip codes in Multnomah and Washington Counties. Data for these zip codes are obtained from Oregon Immunization ALERT.
8. Cost estimate to state general fund—These data were prepared by the Oregon Immunization Program in response to Senate Joint Resolution 1, Legislative Session 2009
9. Minutes from the Immunization School/Facility Law Advisory Committee Meeting, November 13, 2008

Notes:

This document was approved by the Oregon Immunization School/Facility/College Law Advisory Committee, December 9, 2009. The Committee voted 9-1 against requiring HPV vaccine for school attendance at this time. This document is expected to be updated in the future, as recommendations for immunization change and new data become available.