Report of the HPV Vaccine Delivery Meeting

Identifying Needs for Implementation & Research

Geneva, 17-19 April 2012

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1 | Introduction & Background of the meeting

Cervical cancer is the 2nd most common cancer affecting women by age-standardized rate (ASR) for incidence and more than 85% of the global disease burden is in developing countries. The availability of HPV vaccines as a new approach to successfully fight cervical cancer has generated substantial excitement and enthusiasm for introducing the vaccine.

As of the end of 2011, 40 countries had introduced HPV vaccine in their national immunization schedule. Global experience with HPV vaccine delivery to its target population of 9 – 13 year old girls remains limited, particularly in resource-poor settings. Furthermore, there are many stakeholders and partners for HPV vaccine introduction and cervical cancer prevention who are new to immunization and are not the traditional child health partners of immunization programmes, but who bring experience from the fields of reproductive health, adolescent health, school health, cancer control, HIV prevention, and women's health.

In this complex context, there is a need to optimally coordinate the energy, advocacy, and resources of the many stakeholders and partners so that critical vaccine delivery issues are addressed and so that countries can best benefit from the new opportunity that HPV vaccine can offer. This report summarizes key points from presentations and plenary discussions at the meeting. Priorities for action are outlined in section 9.

Objectives

1. To share an update on HPV vaccine introduction issues and the activities of key partners and stakeholders.
2. To determine outstanding questions that need to be addressed for optimal HPV vaccine delivery in countries.

Outcomes

1. A shared vision among public-private partners on short-, medium-, and long-term priorities for HPV activities.
2. A set of prioritized operational research issues that would facilitate HPV vaccine delivery.
3. A mapping of partner efforts and resources to support HPV vaccine introduction.

Participants at the meeting

The meeting brought together immunization, adolescent health, cancer, and education programme specialists from a range of agencies, non-governmental organizations (NGOs), and academic institutions including: UNICEF, UNESCO, UNAIDS, UNFPA, the World Bank, U. S. CDC, the Health Protection Agency, GAVI, Bill & Melinda Gates Foundation, USAID, PATH, Save the Children, Pink Ribbon Red Ribbon Initiative, Union for International Cancer Control, Pathfinder International, Barcelona Centre for International Health Research, Johns Hopkins School of Public Health, and the London School of Hygiene and Tropical Medicine, as well as from four departments within WHO Geneva and from 5 of the 6 WHO regional offices.

2 | The "State of the Science" of HPV vaccines

- Currently there are 2 prophylactic HPV vaccines with high efficacy (>90%) against a variety of vaccine-type-related outcomes: a bivalent vaccine (Cervarix) and a quadrivalent vaccine (Gardasil/Silgard).

- Both vaccines have high efficacy against cervical precancers (CIN2+) due to HPV types 16 and 18. The quadrivalent vaccine also has high efficacy against genital warts due to HPV types 6 and 11 and against anal precancers (AIN2+).

- Approximately 70% of cervical cancers in all regions of the world are due to HPV types 16 and 18; this means that 30% of cervical cancers are from HPV types not included in the 2 currently available vaccines. Cross-protection against infections caused by HPV types not currently in the vaccines and the duration of cross-protection are under study.

- There is no evidence of waning protection over time for either vaccine. Currently, there is information for a post-vaccination follow-up period of 8-9 years.

- Pre- and post-licensure safety data are very reassuring and show an excellent safety profile. HPV vaccines can be co-administered with other vaccines.

- Small studies in HIV-infected persons show that HPV vaccine is safe and immunogenic. However, antibody titers are lower and long-term immunogenicity and duration of protection are unknown. Studies are on-going. There are no contraindications to vaccinating HIV-infected persons with HPV vaccine.

- Use of quadrivalent HPV vaccine for males is recommended in 3 countries (U.S., Australia, and Canada) but publicly funded only in one (U.S.). Decision to recommend the vaccine for males depends on epidemiology of HPV disease in a country, cost-effectiveness, and affordability. For most low and middle income countries, the burden of cervical cancer far exceeds the burden of HPV-associated cancers in males.

- Two-dose vaccination schedules or schedules with longer intervals between doses may be more convenient for vaccinees, providers, and parents and could facilitate implementation and reduce costs. Data from initial, small studies appear promising but are not powered to provide adequate certainty and do not yet answer whether 2-dose schedules will provide adequate long-term protection or whether 2 doses will be sufficient for special populations, such as those who are immunocompromised.

- Substantial vaccine research is ongoing; post-licensure monitoring data and effectiveness data are becoming available. Second generation vaccines are being developed. WHO monitors the availability of new data to determine when global recommendations for vaccine use should be updated.

3 | The "State of the Art" of HPV vaccine delivery: A Work in Progress

- WHO recommends a Comprehensive Approach to Cervical Cancer Prevention and Control with attention to primary prevention (education, HPV vaccination), secondary prevention (screening for early detection and early treatment of precancerous lesions and of early cancer), and tertiary prevention (cancer treatment and palliative care).

- The WHO position paper on HPV vaccine[1] recommends that HPV vaccine be introduced into national immunization programmes where cervical cancer prevention is a public health priority, vaccine introduction is feasible and financially sustainable, and cost-effectiveness has been considered. In addition WHO recommends:
  - Prioritizing high coverage in the primary target population of girls who are 9 to 13 years old.
  - Prioritizing strategies to include populations who are likely to have less access to cervical cancer screening later in life.
  - That HPV vaccine introduction should not divert resources from effective cervical cancer screening programmes.
  - That HPV vaccine should be introduced as part of a coordinated strategy to prevent cervical cancer and other HPV-related diseases.
  - That opportunities to link vaccine delivery to other health programmes targeting young people should be sought.

- HPV vaccine introduction comes with challenges common to any new vaccine introduction: it is necessary to justify that the vaccine addresses a public health priority, to assess costs of the vaccine and of delivery, to consider timeline and coordination with other immunization programme priorities, to create a new vaccine introduction plan and incorporate it into the country's comprehensive multi-year plan (cMYP) for the national immunization programme, and to view the vaccine as part of an integrated disease control approach.

- Challenges that are unique to HPV vaccine introduction are that it needs to be delivered 3 times within 6 months to a new target population, 9-13 year old girls, who have not previously been routinely served by immunization programmes in most countries. In developing countries where this population may be receiving some services related to nutrition, de-worming, vision screening, or malaria prevention or other services, these services are different from delivering HPV vaccine since they typically do not require health workers, injections, or cold chains. Optimal vaccine delivery strategies to routinely reach girls with 3 doses in ways which are acceptable, affordable, and sustainable and which achieve high coverage are still being determined. In any given country, it is likely that combining several different vaccine delivery strategies (e.g. facility-based, school programmes, campaigns) will have to be considered.

- Opportunities with HPV vaccine include the possibility of establishing primary care for 9-13 year old children and harnessing the added energy and advocacy of new stakeholders and partners (in addition to immunization, also partners in adolescent health, school health, reproductive health, HIV prevention, cancer, and women's health) to make HPV vaccine delivery successful.

- Countries that are considering HPV vaccine donations may wish to review the 2010 WHO-UNICEF Joint Statement on Vaccine Donations to consider the recommended requirements that should be satisfied before accepting the donation.

[1] *See http://www.who.int/immunization/documents/positionpapers/en/*

Lessons learned from HPV vaccine introductions

- Global experience with successful and sustained HPV vaccine delivery to 9-13 year olds remains limited. Every country has an array of problems to solve when implementing HPV vaccine; HPV vaccine delivery is unlike anything most immunization programmes have previously done.

- Size of target population and location of target population are often revisited after the 1st and even the 2nd year of HPV vaccination. Delivery strategies are also revised after initial introduction to be able to sustain routine vaccine delivery.

- Costs for both vaccine and for vaccine delivery are significant, and may not be affordable for many developing and low income countries.

- Demonstrating successful delivery of HPV vaccine through demonstration projects using donated vaccine does not assure that HPV vaccine delivery will be sustainable or feasible on a national scale.

- Where schools are used for vaccine delivery, it is necessary to have good coordination at high levels between Ministry of Education and Ministry of Health, engagement and education of local school staff, and both high enrollment and high attendance of girls (in order to have good coverage and achieve affordability). In countries with existing infrastructure (e.g., school health coordinators or school immunization teams), these are useful for HPV vaccine delivery. But in the absence of existing infrastructure or ongoing funding support, using schools for delivery is not always sustainable due to the logistics and costs. Finally, to vaccinate girls who are least likely to access cervical cancer screening later in life, a country cannot rely solely on school-based vaccine delivery.

WHO HPV Vaccine Resources

These and more resources may be found at http://www.who.int/nuvi/hpv/resources/en/index.html

- **Burden of cervical cancer disease** by country may be found on the HPV Information Centre website (http://www.who.int/hpvcentre/)
- For **putting together a national strategy for cervical cancer prevention**, one can use the WHO WPRO November 2009 Meeting Report, Annex 4 and Annex 5, on http://www.wpro.who.int/entity/noncommunicable_diseases/documents/cervical_cancer_meeting/en
- **To estimate costs of HPV vaccine introduction**, one can use the WHO Cervical Cancer Prevention and Control Costing Tool on http://www.who.int/nuvi/hpv/cervical_cancer_costing_tool/en/index.html
- To examine cost-effectiveness, one can review the 2011 BMC Medicine article on use of **cost-effectiveness models for HPV vaccine introduction** in low- and middle-income countries.
- To **assess the readiness of a country's school and health systems to deliver school-based immunization services**, a country may use the School Vaccination Programme Readiness Assessment Tool.
- One can review requirements that should be satisfied before accepting a vaccine donation by reading the **2010 WHO-UNICEF Joint Statement on Vaccine Donations**.

- Investments in effective IEC (Information, Education, and Communication) are critical for HPV vaccine.

- Effective follow-up systems are needed in order to reach missed girls and to reach girls again in order to deliver 2nd and 3rd doses.

Monitoring and evaluation of HPV vaccine delivery

- HPV vaccine coverage monitoring by dose and by year of age is necessary for programme assessment and for vaccine impact monitoring and to allow comparison of vaccine coverage trends over time and across geographical areas.

- A critical issue for HPV vaccine coverage is that the denominator should be the total number of girls in a given geographic area by year of age. A denominator of total girls enrolled in school describes coverage for a school vaccine delivery strategy but does not describe coverage for the eligible target population.

- WHO has developed HPV Vaccine Coverage Monitoring Guidance with tally sheets for country use, as well as guidance on conducting an immunization coverage cluster survey for HPV vaccine.

- Through the annual WHO-UNICEF Joint Reporting Form that is used to collect vaccine coverage data, countries should report data on numbers of HPV vaccine doses administered.

- WHO recommends that countries conduct Post-Introduction Evaluations (PIEs) approximately 6-12 months after introducing any new vaccine in order to assess delivery of the new vaccine. A PIE is an on-site assessment of all aspects of vaccine delivery (training, supervision, communication, cold chain, access to target population, acceptability by population, etc.) with the goals of identifying programmatic gaps and of making improvements to the vaccination programme. Countries can request support for conducting a PIE through their WHO Country and Regional Offices.