

## **Concerns around HPV vaccine: A Memorandum to the Health Minister**

In a Memorandum to the Ministry of Health and Family Welfare, public health activists, along with several health networks and organisations, voiced concerns around the introduction of the Human Papilloma Virus (HPV) vaccine Gardasil.

The Memorandum is as follows:

To  
Shri Ghulam Nabi Azad,  
Union Minister for Health and Family Welfare,  
Ministry of Health and Family Welfare,  
Nirman Bhavan,  
Maulana Azad Road,  
New Delhi 110 011

Date: October 1, 2009

Subject: Concerns around Human Papilloma Virus (HPV) vaccine

Sir,

We, the undersigned, public health organizations, health networks, medical professionals and women's groups, write to express our concern with regard to the introduction of Human Papilloma Virus (HPV) vaccine, Gardasil, to young girls in the country.

On July 9th, 2009 under the demonstration project being implemented by the Union Ministry of Health and Family Welfare in association with Indian Council of Medical Research (ICMR), PATH International and State government, the Andhra Pradesh Minister for Health and Family welfare launched a pilot program for vaccination against cervical cancer. The three doses of HPV vaccine are to be administered to 16,000 girls between 10 and 14 years in the mandals of Bhadrachalam, Kothagudem and Thirumalayapalem in Khammam district in Andhra Pradesh.[1] The vaccine will be administered in 3 doses at the interval of 0, 2 and 6 months.

Similarly, on August 13, 2009, the Gujarat government launched a two-year 'Demonstration Project for Cancer of the Cervix Vaccine' in three blocks of Vadodara District – Dabhoi, Kawant and Shinor – to immunize 16000 girls between 10 and 14 years with three doses of Gardasil. The Gujarat State Minister for Health and Family Welfare claimed that this demonstration project will help the Centre to examine the possibility to introduce the vaccination project across the country [2]

We are alarmed by this decision by State and Union Governments and we oppose the introduction of the vaccine on the following grounds:

### **Efficacy of the Vaccine**

- Information about the efficacy of Gardasil remains uncertain. The current HPV vaccine prevents infections, resulting from just two of the HPV subtypes (16 and 18) that may cause cervical cancer, and also HPV subtypes 6 and 11 that can lead to

genital warts. The subtypes 16 and 18 account for 70% of the cases of invasive cervical cancer globally.[3] But there are over 100 HPV subtypes and one of the main concerns is that if the vaccine was to work and indeed 'block' subtypes 16 and 18 then the other carcinogenic subtypes may become dominant.

- There is lack of conclusive data regarding the length of immunologic protection the vaccine confers against HPV subtypes 16 and 18.[4] Studies so far have followed up with the vaccinated 'subjects' for 5 years and have shown that it offers protection only for 5 years. Thus it is not clear whether protection lasts longer than this time period. Since the long term efficacy and protection by the vaccine is unknown we can not claim that even 60-70% protection will be achieved. Moreover, since the highest incidence of cancer of the cervix in India is in women above 35years of age, it is not clear whether a 3-dose schedule will provide long lasting immunity or if boosters will be required.
- If booster doses are needed, and it is not known how frequently, what will be the impact of the booster doses on the safety of the vaccine? Moreover, booster doses would certainly increase the cost of vaccination per woman as many times as the booster would be given.
- HPV vaccination is not a substitute for cervical cancer screening. All women, including those who are vaccinated, should continue to have regular Pap test screening and also HPV test as the preventive effect of the vaccine on cervical cancer has not yet been demonstrated.
- HPV Infection rarely leads to progression to cancer. Only a minority of infections persist for several years, and only about 10% of low-grade lesions progress to a higher grade. About 5% of high-grade lesions progress to invasive cancer.[5]

### **Side-effects**

The Federal Vaccine Adverse Event Reporting System (VAERS) in the US has logged a total of 12,424 of adverse events following HPV vaccination, according to the US Centre for Disease Control and Prevention. Between June 2006 through December 2008, more than 23 million doses were administered in the US alone. Of these, 772 were reports of serious events (6.2 % of the reports) including 32 deaths and the remaining 11652 (93.2%) were classified as non-serious.[6]

The most common events reported were, Syncope, Local reactions at the site of immunization (pain and redness), Dizziness, Nausea and Headache.[7] Venous thromboembolic events, autoimmune disorders, Guillian Barre Syndrome, motor neuron disease, anaphylaxis, transverse myelitis, pancreatitis and death were amongst the serious adverse events reported. Amongst reports of autoimmune disorders to the VAERS system, 88% were associated with the HPV vaccine alone.[8]

1. In Australia, the rate of anaphylaxis shock after Gardasil injection has been reported as 2.6 per 100.000 doses[9].
2. The official Gardasil website itself clearly mentions, "GARDASIL may not fully protect everyone, and does not prevent all types of cervical cancer, so it's important to continue routine cervical cancer screenings. GARDASIL does not treat cervical cancer or genital warts".[10] The side effects listed include, pain, swelling, itching,

bruising, and redness at the injection site, headache, fever, nausea, dizziness, vomiting, and fainting. Sometimes fainting is accompanied by falling with injury, as well as shaking or stiffening and other seizure-like activity.[11]

3. The Indian Academy of Pediatrics Committee on Immunization (IAPCOI) in their recommendations mentions that, the vaccine is contraindicated in those with history of previous hypersensitivity to any vaccine and should be avoided during pregnancy.[12] Moreover, there have been no adequate and well-controlled studies in pregnant women, and animal reproduction studies are not always predictive of human response.[13]

Moreover, while this data is mostly sourced from US based research and trials conducted in other countries, the adverse reactions in the Indian context are unknown. Thus, the approval of a vaccine that claims to prevent a sexually acquired infection that sometimes causes cancer of cervix, and that too only if vaccination is completed before exposure, is highly questionable.

### **Cost Effectiveness**

- The current cost of the vaccine is Rs. 3000/- per dose (approximately USD 60) per dose. So for every 10-year old girl, 3 shots initially, and 8 shots (assuming the need for a booster shot every 5 years) over the next 40 years [until she becomes 50]. This would amount to Rs. 33,000/- by present estimate. Can the Ministry afford an injection that costs Rs 9,000 for every woman in a country where we cannot give DPT (costing Rs. 3) to 50% of children of the country?
- In a recent study from India, published in the New England Journal of Medicine (NEJM), 31,488 women (30 to 59 years old), were followed up over 8 years with no intervention (in the control group). 64 died of cervical cancer. The absolute risk of cervical cancer was 2.5/10,000/year. If we optimistically assume that every case of cervical cancer will be prevented by the vaccine, the absolute risk reduction is 0.00025 and the numbers of women needed to be vaccinated to prevent one death is 4000. So the cost per life saved is Rs. 75 million.[14]
- A cost effectiveness study published in the NEJM in 2008 concluded that if the vaccine provided protection against HPV for only ten years, then vaccinating preadolescent girls would only provide a “2% marginal improvement in the reduction in the risk of cervical cancer as compared with screening alone.” Moreover, it would cost \$144,100 for each healthy year of Life Saved, instead of the \$ 43,600 estimated for a vaccine providing life-long protection. Most researchers believe that even in the US, interventions costing more than \$50,000 per quality-adjusted year of life (QALY) saved, are not cost-effective, while others use a higher ceiling of \$100,000.[15]
- Looking at our public health system, no government in India can afford this expense. The average per capita annual income in India in 2009 is Rs.38 000 and, while the current per capita annual public health expenditure in India is about USD 10.
- Given this totally unfavorable cost-efficacy in the Indian context, we see no chance that this vaccine can be included in the Indian National Immunization program. Hence

conducting such a demonstration project in India would mean using Indian people as mere guinea pigs.

### **Aggressive Marketing**

- Merck Sharp & Dohme (MSD) India Pharmaceuticals Private Limited, which is the Indian subsidiary of Merck & Co. Inc., the manufacturers of Gardasil, has also recently started a Cervical Cancer Prevention Program that informs Indian Women to help protect them against cervical cancer and related HPV infections. The program's tagline, "What will I do to save my daughter from cervical cancer? – Everything that I can!"[16] is uncannily similar to Gardasil's tag line – "We chose to help protect ourselves against cervical cancer and other HPV infections: Now the choice is yours."[17] Similarly, PATH, that supported the formative research for the HPV vaccine Gardasil in India, highlights the demand for the vaccine through quotes like "Our granddaughters' generation should be a generation without cancer."[18] In this way a false signal is sent out that claims that the vaccine can prevent cancer although Gardasil prevents cancer of cervix associated with just 2 types of HPV.
- These advertisements induce fear with regard to HPV and cervical cancer and thus create an inaccurate impression of a "public health emergency".
- A 15-second commercial on Indian television urges parents to get their young girls inoculated with the vaccine Gardasil to protect against cervical cancer, Advertising prescription drugs on television is unethical enough, but using fear and inaccurate claims to sell them is worse.[19]

We urge that

The Government should review the decision to conduct a demonstration project of HPV vaccine in the mass immunization programs in the absence of sufficient long-term evidence of its effectiveness complete and unbiased information, and without any prior public debate. The huge cost incurred in this mass immunisation even if the current price of the vaccine is reduced substantially should be seriously considered.

The state initiates comprehensive access to reproductive and sexual health programs / services for adolescents, women and men.

- The focus should be on increasing access to preventive health care services such as pap screenings, visual screening of the cervix with acetic acid (VIA) and Visual Inspection of cervix with Lugol's Iodine (VILI).
- Screening programs should be augmented with newer technologies such as the use of liquid based pap testing in women, who have abnormal pap test results.
- Provide population-based outreach pap screening services for Cancer of cervix, particularly for women from the tribal and rural areas.
- Undertake special measures towards promoting awareness among women and community so that they come forward without any inhibitions to undergo such screening tests.
- Instead of an expensive vaccination strategy, monitoring measures should be made available to detect Cervical Cancer at a very early stage. Treatment of all

women with the diagnosis of Cervical Cancer in situ is likely to cost the public health care system much less, than buying the vaccine.

- Public health services be made available to all, with special emphasis on women's health, by filling in the vacancies of the gynaecologists and para- medical workers, by providing basic screening facilities.

As mentioned earlier the current vaccines target only 2 oncogenic types: HPV-16 and HPV-18. Secondly, the relationship between infection at a young age and development of cancer 20-40 years later is not known. So how should a parent, physician, politician, or anyone else decide whether it is a good thing to give young girls the vaccine that partly prevents infection caused by a sexually transmitted disease that in a few cases will cause cancer 20-40 years from now?[20]

It is learnt that the Union Health Ministry has signed a memorandum of understanding (MoU) with the US Company Merck, covering the entire gamut of the trial and the launch in the country. As per the MoU, the pre introductory trial will be carried out at several centres in the country, including Institute of Cytology and Preventive Oncology (ICPO) ([www.icpo.org.in](http://www.icpo.org.in)) for a duration of 6 months. What is the status of these trials and if they have been completed, what are the results / findings?

Financial support from industry or from an international organization should not be the criteria to introduce any vaccine in pilot phase or in universal immunization program. The role of PATH is not very clear. It appears that PATH is trying to find ways of influencing policy makers through its formative research.

### **Our Demands;**

1. All trials and studies to be immediately brought to a halt till in an open forum questions relating to safety, efficacy and cost effectiveness of the planned intervention can be justified.
2. To place before the public:
  - All the documents pertaining to the agreement with vaccine manufacturers and all other bodies regarding the government's plan to introduce the HPV vaccine. The list of all trials planned, proposed, approved and completed, the agencies involved, the donors involved and proposed locations and all the results of the pilot phase trials as well as clinical trials.
  - The status of approval accorded to the vaccine and the data which has been submitted by the company (vaccine manufacturer) for the purpose.
  - The estimated total cost, as per the government's assessment, of purchase of the vaccine and its administration.
3. A vaccine policy to be formulated based on public health needs.
4. Open up the issue for public debate and the opinion of health groups, women's groups and other civil society members to be actively sought.

We urge you to consider these demands very seriously and act upon this matter in the larger interest of the health and well-being of the women and adolescent girls of this country. We

ask you to provide the information and documents that we have requested within a month of the receipt of this letter.

Yours Sincerely,

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Medico Friend Circle (MFC)  
Jan Swasthya Abhiyan (JSA)  
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Taken from Sama (A Resource Group for Women and Health) Website:

<https://samawomenshealth.wordpress.com/2009/12/14/concerns-around-hpv-vaccine-a-memorandum-to-the-health-minister/>