

**Memorandum of Concerns Regarding the Interim Report of the Committee Appointed by the Government of India to Enquire into “Alleged irregularities in the conduct of studies using Human Papilloma Virus (HPV) vaccine”**

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Shri Ghulam Nabi Azad,  
Union Minister for Health and Family Welfare,  
Ministry of Health and Family Welfare,  
Nirman Bhavan, Maulana Azad Road,  
New Delhi 110011

Date: 21st February, 2011

Subject: Concerns regarding the Interim Report of the Committee appointed by the Government of India to enquire into “Alleged irregularities in the conduct of studies using Human Papilloma Virus (HPV) vaccine” by PATH in India.

Sir,

We, the undersigned public health organizations, health networks, medical professionals, human rights groups and women’s groups write to voice our deep concerns regarding the Interim Report of the Committee appointed by the Government of India (vide notification No. V.25011/160/2010-HR dated 15th April, 2010) to enquire into “Alleged irregularities in the conduct of studies using HPV vaccine” by PATH in India.

While identifying several deficiencies in the planning and implementation of the project, the report, submitted to the Ministry of Health and Family Welfare, has failed to fix responsibility on any individual or agency. Rather than suggesting any punitive or disciplinary measures, the report identifies ‘minor’ deficiencies as lessons for strengthening clinical research in future.

**Our questions and concerns**

The report does not contain accounts of any interaction with the participants of the study (either in Gujarat or AP), their parents, the hostel wardens, teachers, local health workers etc, or even with the parents of the girls who died post vaccination for verbal autopsies of the deaths. These do not appear to have taken place, and may be considered a significant methodological limitation of the report.

In marked contradiction to the official stand of both PATH and ICMR, the report states that: “It needs to be highlighted that 4 of the 5 primary outcome measures proposed in the study relate to evaluation of the safety of the vaccine.” For instance, in an update posted by PATH on their website (accessed on 15 February 2011) following the suspension of the projects, they state,

“It should be noted that the post-licensure observational studies in Andhra Pradesh and Gujarat do not seek to evaluate the efficacy or safety of these licensed, approved HPV vaccines. No biomedical outcomes are being researched; no blood or other samples are being drawn, and no therapies are being tested. The safety and efficacy of these vaccines have been documented in numerous studies and endorsed by numerous international and national

regulatory agencies.” Similarly, in the response from Mr. A.B. Ramteke, Joint Drug Controller (I) to an RTI (dated 21.07.2010), it was clearly stated that the design and purpose of the study was i) to demonstrate suitable vaccine delivery strategy ii) to raise community awareness iii) to build the evidence base of vaccine delivery strategy for future introduction of HPV in India. However, it was not mentioned that the study outcome was to evaluate the safety of the vaccine.

Not only does this reveal the inconsistencies in the literature made available in the public domain regarding the nature, aims and outcomes of the projects, moreover, if the safety of the vaccine is in fact being studied, it may be ascertained that the projects are clinical trials. Thus, the protocols of clinical research in India have been violated. The Committee has not dispelled this ambiguity.

The report states, “One of the major deficiencies of the study in retrospect was inadequacy of the preparation for tackling Serious Adverse Events (SAEs) and deaths, whether related or unrelated to the vaccine. The deaths came to notice after a long gap of their occurrence, mainly when the preparations were a foot for the next round of vaccination. And then no independent body of experts analyzed the cause of deaths.” In the absence of any mention of the follow up of deaths and serious adverse events, how did the State governments and other authorities[1] approve the study design? Further, deaths and adverse events following vaccine administration were not investigated by the DIO or DRCHO. The Drugs and Cosmetics Act clearly outlines that ethics committees are responsible for review and approval of trial protocol so as to safeguard the rights and well-being of trial subjects, especially those from vulnerable sections of the population. There appears to be reluctance to hold the involved ethics committees accountable for violations.

We welcome the recommendation for “the need for continued pharmacovigilance of the HPV vaccine” and the reiteration of rule 122-E of the Drugs and Cosmetics Act, that “all vaccines, in particular the HPV vaccine, shall be treated as new drug for four years from the date of their approval in India. All research studies (whether a clinical trial or not) involving administration of a new drug (vaccine), even after licensing, should proactively monitor and investigate all adverse events, more so the SAE and deaths irrespective of their appearing or not appearing to be related to the vaccine.”

Further, while the Interim Report justifies the inclusion of girls in the age group of 9-14 years in the PATH projects as bridging the Phase III trials conducted prior to the approval of the drug for marketing, sale and import for private markets in India, it completely ignores the inadequacies and shortcomings of these pre-trials themselves.

While the report states that “there was no specific targeting of any particular group or class except that the plan called for including a predominantly urban, rural and tribal block in each selected district”, it goes on to say that “in hindsight the veracity of this plan can be debated... . . . if it was impractical to take consent of parents in predominantly tribal area such an area might have been excluded from the study.”

The report establishes that “The legality and morality of the circular of the Government of Andhra Pradesh authorizing the Hostel Wardens and Head Masters to sign the consent on behalf of the minor girls included in the study is questionable.” This is an absolute travesty of free and informed consent, a central and inviolable tenet of research ethics, as listed in both the DCA and ICMR’s ethical guidelines for biomedical research.

The report states that “no provision has been made of an insurance cover for any unforeseen event (including death) or residual morbidity related to the intervention for vaccine recipients in this study which is the usual practice for trials with NCE/ INDs”. It goes on to establish that “PATH has taken an insurance cover for itself”. In this case, why were the participants not covered? Further, the absence of any mention in the study protocols of an insurance cover for participants raises concerns regarding the inadequacies of the approval processes, and the responsibilities of the approval bodies.

The Committee has noted that the use of the State’s health machinery for the execution of the project “might have led to blurring of the distinction between routine, national immunization programme and research nature of the HPV vaccination study”. As such, “it is important for Public Private Partnership programmes to be extra vigilant and ensure that the Authority of the State is not misrepresented.”

Despite stating that “the fact that the vaccine for the study was provided by manufacturers free of cost does raise the concern about undeclared conflict of interest since the results of the study may be used to influence the decision by the Government”, the Committee fails to build upon this significant and alarming aspect.

The section of the report on Responsibility is the weakest, as it lets off the hook all those involved in the project, by declaring the deficiencies in the project as “minor” and not “willful or fully anticipable (sic)”, and stating that “since there does not appear to be any overt mal-intention, no responsibility can be fixed”.

### **Our demands**

1. Since violations have occurred at all levels of the project, we demand that all involved be considered culpable, and appropriate punitive action be taken. To say that responsibility cannot be fixed with any “one” individual or organization is a dereliction of duty, and a convenient excuse for irresponsible and unethical conduct, thus setting a dangerous precedent.
2. Compensation should be provided, with immediate effect, to the families who have lost their children and to the children suffering side-effects.
3. All study participants should be provided proper medical treatment and follow up
4. The Government should place in the public domain:
  - 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 and design of projects planned, proposed, approved and completed, agencies involved, and donors involved, proposed locations, and all the results of the pilot phase and clinical trials.
  - All details, including names and minutes of the meetings, of all ethics committees that approved or disapproved the study plan.

- The full version of the Interim Report by the Government of India inquiry committee, as soon as it is ready.

We hope you will take cognizance of our demands, and appropriate action.

Signed By:

1. Jan Swasthya Abhiyan (Indian chapter of the People's Health Movement)
2. Sama- Resource Group for Women and Health
3. Saheli Women's Resource Centre
4. Low Cost Standard Therapeutics
5. All India Democratic Women's Association
6. All India People's Science Network
7. National Federation of Indian Women
8. Jagori
9. Haq: Centre for Child Rights
10. Gramya Resource Centre for Women
11. Dr. Imrana Qadeer
12. Dr. Indira Chakravarthi
13. Rajashri Dasgupta
14. Veena Shatrugna

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[1] 1. National Advisory Group constituted by ICMR, 2. State Advisory Group of AP and Gujarat, constituted by the State governments, 3. Health ministry's Screening Committee of the Government of India, 4. DCGI- license for import of vaccine for trial and trial protocol, 5. Institutional Ethics Committee of NARI for Phase I study, 6. Institutional Ethics Committees, separately for AP and Gujarat, for Phase II study, and 7. Western Institutional Review Board, an independent ethics committee based in Olympia, WA, USA

\*Excerpts of this memorandum have been published in the Medico Friend Circle Bulletin

Taken from Sama (A Resource Group for Women and Health) Website:

<https://samawomenshealth.wordpress.com/2011/04/23/memorandum-of-concerns-regarding-the-interim-report-of-the-committee-appointed-by-the-government-of-india-to-enquire-into-%E2%80%9CAlleged-irregularities-in-the-conduct-of-studies-using-human-papillom/>