Trials and tribulations: an expose of the HPV vaccine trials by the 72nd Parliamentary Standing Committee Report

N SAROJINI, V DEEPA

Sama-Resource Group for Women and Health, B 45, Shivalik Main, Malviya Nagar, New Delhi -110017 e-mail: sama.womenshealth@gmail.com

Background

In mid-2009, the human papillomavirus (HPV) vaccine "demonstration projects" were conducted by the Program for Appropriate Technology in Health (PATH), a Seattle-based non-governmental organisation, in collaboration with the Indian Council of Medical Research (ICMR) and the state governments of Andhra Pradesh and Gujarat. The projects were funded by the Bill and Melinda Gates Foundation. The vaccines used, Gardasil and Cervarix, were donated to PATH by the manufacturing companies; in this case, GlaxoSmithKline and Merck Sharp and Dohme (MSD). These HPV vaccines were administered to approximately 23,000 young girls, of between 10 and 14 years of age, in the district of Khammam in Andhra Pradesh, and in the district of Vadodara in Gujarat.

These projects were suspended by the ministry of health and family welfare (MoHFW) in 2010, following the deaths of seven tribal girls and strong opposition from civil society groups to the unethical design and conduct of the projects. An inquiry committee was constituted to look into the "alleged irregularities" in the conduct of the projects. The committee's report (1) agreed with the contention that there had been several violations of the rights of the participants and of regulatory procedures, but failed to apportion blame. It also remained silent on the recommendation that those involved in permitting and conducting such a trial should be punished. Despite evidence of clear violations, the inquiry absolved all involved in the project of any responsibility.

Taking a serious view of the procedural and ethical lapses in the projects, the 72nd Parliamentary Standing Committee on Health and Family Welfare recently carried out an enquiry into the studies and presented its report on "Alleged Irregularities in the Conduct of Studies using Human Papilloma Virus (HPV) Vaccine"(2), in the Rajya Sabha on August 30, 2013. This report (henceforth referred to as the 72nd Report) (2), is a clear and comprehensive vindication of the many voices and the campaign that have consistently drawn attention to violations in HPV vaccine trials in India. The 72nd Report acknowledges the unethical nature of the HPV vaccine "demonstration" project conducted in the country in 2009 by PATH (2).

Undoubtedly a clinical trial

The 72nd Report clearly states that the "demonstration project", as it was repeatedly referred to by PATH, was a clinical trial, regardless of what PATH called it (2). The report takes note of the observations of the MoHFW's enquiry committee that, "the demonstration project is a study of a pharmaceutical product carried out on humans and since the primary objectives include the study of serious adverse events, it is clear that clinical trial rules and guidelines should apply" (2:p14).

The 72nd Report further states that by carrying out the clinical trial in the guise of an "observation/demonstration project," PATH has violated all the laws and regulations laid down for clinical trials by the Government of India (2).

Dereliction of duty and other serious concerns

Unlike the report of the MoHFW's enquiry committee (1), however, the 72nd Report points to serious dereliction of duty on the part of many of the institutions and organisations that were involved (2:p 21), in particular the ICMR, the Drugs Controller General of India (DCGI), Ethics Committee (EC) members and PATH.

The 72nd Report questions the role of the ICMR, the apex body in the country for health research and the formulation of guidelines on clinical trial ethics, which was a complicit participant and collaborator in this project (2). The 72nd Report states that the ICMR Project Advisory Group (PAG) representative and some of the council's officials acted as partisans of PATH and in the interest of the manufacturing companies, rather than as representatives of an institution mandated to maintain as well as ensure the implementation of the highest ethical standards in research (2:p21).

The 72nd Report also mentions that one of the roles assigned to the ICMR as per the memorandum of agreement (MOU) signed by the Director-General of the council is "advising on plans for results dissemination to support decision-making for use of the HPV vaccine." (2). The Report expresses its inability to "understand as to how ICMR could commit itself to support the use of the HPV vaccines in an MOU signed in 2007, even before the vaccine was approved for use in the country." It also wonders "how the ICMR could commit itself to promote the drug for inclusion in the Universal Immunisation Programme (UIP) even before any independent study about its utility and rationale for inclusion in the UIP was undertaken" (2:p19).

The Standing Committee's inquiry has proved that the DCGI played a very questionable role in the entire matter. According to the 72nd Report, the DCGI "remained a silent spectator even when its own rules and regulations were being so flagrantly violated." The report further states: "The approvals of the clinical trials, marketing approvals and import licences by the DCGI appear irregular" (2:p24).

The Standing Committee has firmly rebuked the Department of Health Research under the MoHFW. According to the 72nd Report, "the whole issue has been diluted and no accountability has been fixed on the erring officials/department for gross violations committed in the conduct of the study." The committee also felt that a very casual approach had been taken by the department in the matter and that its response reflects the lack of any concrete action to protect and safeguard the health of our people (2:p37).

Questioning the role played by PATH, the Standing Committee report states, "It is apparent that PATH has exploited with impunity the loopholes in our system, as also the absence of a nodal point or a single window for maintaining a data bank of foreign entities entering the country for setting up their offices" (2:p41). It goes on to say, "…it is established that PATH, by carrying out the clinical trials for HPV vaccines in Andhra Pradesh and Gujarat under the pretext of an observation/demonstration project, has violated all laws and regulations laid down for clinical trials by the government. While doing so, its sole aim has been to promote the commercial interests of HPV vaccine manufacturers who would have reaped windfall profits had PATH been successful in getting the HPV vaccine included in the UIP of the country" (2:p42).

The Standing Committee takes a serious view of the violations and strongly recommends that on the basis of the facts, PATH should be made accountable and the MoHFW should initiate appropriate action in the matter. This should include legal action for the breach of various laws of the land and possible violation of the laws of the country of PATH's origin (2:p30; pp 42–43).

Conflict of interest

The Standing Committee sought information from the MoHFW as to whether the members of the inquiry committee were asked to file a conflict of interest declaration. According to the 72nd Report, MSD was sponsoring and funding a trial in the All India Institute of Medical Sciences (AIIMS), in the department to which a member of the inquiry committee belonged (2). The report further states: "This demonstrates a serious conflict of interest of this member of the inquiry committee" (2:p26). The Standing Committee has strongly deprecated the government's action in "appointing the committee to inquire into such a serious matter in such a casual manner even without ascertaining as to whether any of the members of the said inquiry committee have any conflict of interest with the subject matter of the inquiry" (2: p27).

The 72nd Report states: "The ministry appointed a senior official of ICMR (described as resource person) to assist the inquiry committee. The concerned individual was the main link between ICMR and PATH, and had participated actively in all discussions and meetings and helped PATH to carry out the project proactively in every respect right from the beginning in October 2006. As such, he had a clear conflict of interest and could not be relied upon to give correct information and unbiased opinions. Indeed, he should have been summoned as a witness to answer questions and not as an official resource person attached to the enquiry committee" (2:p26).

Flaws in "project" design, consent process

The 72nd Report expresses its disapproval of the "project" design, which resulted in gross under-reporting of adverse events, and questions the figures for the reported non-serious adverse events (2). It is also critical of the lack of independent systems and rigorous monitoring and management of adverse events/serious adverse events (AE/SAE).

On the issue of consent, the 72nd Report observes that there were gross violations of the concept of consent and the legal requirement for it (2). This is evident from the "incomplete and inaccurate" consent forms, the failure to give comprehensive information to the participants' parents/guardians on various aspects of the vaccination, direction by the state (Andhra Pradesh) to hostel wardens to sign the consent forms on behalf of the parents/guardians, among other things. Another serious gap mentioned by the 72nd Report is the absence of insurance cover for the girls (2).

Funding of the trial: grey areas

The 72nd Report notes the observations made by the inquiry committee at its meeting on September 27, 2010 (Appendix 20.5):

….The study was initiated by PATH on its own … without any reference from the National Technical Advisory Group on Immunisation (NTAGI), the official body of the GOI on vaccines…. It is not clear whether the state expenses were funded by PATH or came from their own resources. The monetary contributions of ICMR are also not clear. The Committee, therefore, felt that it would be in the fitness of the inquiry to document the sources and magnitude of funding of the study (2:p18).

However, the committee's report did not delve into the matter. No mention was made of the funding from the Bill and Melinda Gates Foundation and other sources, or of the money spent by the ICMR and state governments.

Human rights violations

The 72nd Report states that what PATH did is a clear-cut violation of the human rights of girl children and adolescents, and is a serious breach of medical ethics (2). The Standing Committee recommends that "the National Human Rights Commission (NHRC) and National Commission for Protection of Child Rights (NCPCR) may take up this matter further from the point of view of violation of human rights and child abuse" (2:p42). The Committee is of the view that since the population under study was vulnerable, the utmost caution should have been exercised in the implementation of the study.

The 72nd Report (2) emphasises that all guidelines and statutory requirements applicable to research on human participants should have been followed. It recommends that every effort should be made to expedite the preparation of a report that brings to light the real facts about the HPV vaccine trial, and to ensure that corrective measures, both in connection with the HPV trial as well as all such ongoing or proposed clinical trials of drugs/vaccines are implemented.

Conclusion

The 72nd Report (2) validates the campaign led by civil society that has highlighted the violations committed in the HPV trials and has been demanding action ever since deaths were reported in 2010. We hope that the government and agencies concerned will act on the Standing Committee's findings expeditiously. We are living in a world in which scientific and technological advances are being made at a rapid pace and hold great promise; indeed, clinical trials are necessary if safe and effective medicines are to be developed. However, we cannot allow the pharmaceutical industry to go further in the direction in which it seems to be headed today, ie where medical ethics, rules and human rights are sacrificed at the altar of profiteering.

References

1. Final Report of the Committee appointed by the Government of India (vide notification No. V 25011/160/2010 –HR dated April 15, 2010) to enquire into "Alleged irregularities in the conduct of studies using Human Papilloma Virus (HPV) vaccine by PATH in India". New Delhi: GoI; 2011 Feb 15.
2. Department-related Parliamentary Standing Committee on Health and Family Welfare, Department of Health and Family Welfare. Seventy second report on alleged irregularities in the conduct of studies using Human Papilloma Virus (HPV) vaccine by PATH in India. New Delhi: Rajya Sabha Secretariat; 2013 Aug 30 [cited 2013 Sep 17]. Available from: http://164.100.47.5/newcommittee/reports/EnglishCommittees/Committee%20on%20Health%20and%20Family%20Welfare/72.pdf
3. Department-related Parliamentary Standing Committee on Health and Family Welfare. Fifty ninth report on the functioning of the Central Drugs Standard Control Organisation (CDSCO). New Delhi: Rajya Sabha Secretariat; 2012 May 8[cited 2013 Sep 17]. Available from: http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf

ERRATA: *IJME* (JULY-SEPTEMBER 2013)

1. AEFI and the pentavalent vaccine: looking for a composite picture, page 144, para 10, Line 5 should read: "350 lives will be lost to Hib pneumonia and meningitis over the next 5 years by not vaccinating one birth cohort in India."

2. National Vaccine Policy: ethical equity issue, Page 188, Figure 1: The following caption should appear below Figure 1: "From: Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009). Preferred reporting items for Systematic Reviews and Meta-Analyses. The PRISMA Statement. PLoS Med. 6(6): e1000097. doi.10.1371/journal.pmed.1000097'. For more information visit www.prisma-statement.org"

3. Innovations in monitoring of adverse drug reaction: the role of a technical advisor, Page 190: The names of the authors should read as follows: "S RAMALINGAM, TK PONNUSWAMY, YS SIVAN"

4a. Symposium on bioethics: empowerment of research participants/patients, Page 204: The first author's name should read: "S Swarnalakshmi."

4b. Pg 205, column 2, paragraph 3, line 10 should read: "Dr Nandini said that the US Commission for the Study of Bioethical Issues discussed that the US too should have a policy on compensation, as is being discussed in countries like India."

4c. Pg 205, column 2, paragraph 4, line 2 should read: "Dr S Swarnalakshmi, IRB Manager, YRG CARE and Organizing Secretary, TYBS 2013, spoke on PRIM&R, which had co-sponsored the symposium through the regional connections programme."

5. Evolving roles of ethics committees in India, Page 206, Column 1, paragraph 5, lines2-3 should read: "It was suggested that Strategic Initiative for Developing Capacity in Ethical Review, of which the Forum for Ethical Review Committees in Asia and the Western Pacific is a branch, could act as a body to certify many ECs. The Indian Society for Clinical Research (a private organisation established in 2005) is industry-supported but not an industry association.."