

The Conflicts of Interest in the Development and Approval of HPV Vaccine

Whilst it is considered necessary for the manufacturers of drugs to fund the development and approval of their own products it is important that there is an independent assessment of the design of the trials and the safety and efficacy data that has been collected. The public must request that the government demonstrates that its decision to approve HPV vaccine to all Australian adolescents has been based upon balanced and unbiased information.

Below are some facts revealing the conflicts of interests that were declared in the development and approval of the HPV vaccine – a vaccine for which the benefits and risks of protecting against 2 of 20 cancer causing strains of HPV are still undetermined in 2013 (17):

Development of the Vaccine:

- CSL (pharmaceutical company) funded the research for the development of this vaccine at the University of Queensland 18
- Clinical trials for the vaccine were funded by Merck (manufacturer of the vaccine) (13) and the study was designed, managed, and analysed by Merck in conjunction with external academics 6.

The conflicts of interest of the academics include:

1. Indiana University declared that Merck had signed a confidential agreement that pays the university on the basis of certain landmarks regarding HPV vaccine 6
2. 10 authors of the clinical trials were current or former employees of Merck and 18 other authors, including Bosch, Villa and Munoz (the researchers who claimed HPV 16/18 are the determining and independent cause of cervical cancer) reported receiving consulting fees and having served on paid advisory boards for Merck 6.
3. Some trial investigators had also received consulting fees and served on the advisory board for GlaxoSmithKline (GSK) 6

4. Dr. Bosch had received consulting fees and served on the advisory board for GSK and Digene and he had also received lecture fees from Merck and GSK. Research grants were also provided to him from Merck and GSK through his institution to fund the vaccine trials and the epidemiological studies 6.
 5. 11 of the authors including Villa and Munoz received lecture fees from Merck, Sanofi-Pasteur, and Merck Sharp and Dohme 6
 6. Dr. Brown and Dr. Skjeldestad received funding from Merck for natural history studies of HPV infection. Dr. Myers received funding from Merck for conducting modelling studies of the effectiveness and cost-effectiveness of the vaccine in different settings.
 7. 17 authors received funding from Merck through their institutions to conduct clinical trials of the vaccine 6
- In 2005 CSL also entered into a cross-licensing agreement with GlaxoSmithKline, the pharmaceutical company producing the competitor HPV vaccine: Cervarix 19
 - From 2003 – 2007 Gardasil was tested for efficacy against pre-cancerous lesions but safety data comparing vaccinated and unvaccinated groups was not collected for this time period 13. There are no long-term studies (1-3 years) of all the health outcomes from the use of Gardasil.
 - Cervical Cancer takes 8 - 25 years to develop and most pre-cancerous lesions in young women are not an indicator of cancer later in life 3. In addition, HPV infection on its own does not progress to cancer 3 therefore the benefits and risks of this vaccine are still unknown in 2013 17.

The Registration and Approval of Drugs by the FDA

HPV vaccine was approved by the FDA in 2006 14.

The pharmaceutical industry is the largest lobby group in Washington. In 2002 there were 672 lobbyists which meant more than one for each member of Congress 25. Lobbyists are also well connected as many have been members of Congress or held other government positions 25.

There is a revolving door between Congress and pharmaceutical industry boards in addition to the huge political donations that the pharmaceutical companies provide to the major parties 25. This guarantees that pharmaceutical interests will be promoted in all areas of Congress 25.

The favors that this practice has provided include:

1. Legislation to extend drug monopolies
2. Huge tax breaks to the most profitable corporations
3. A law to prevent cheaper drugs being brought into America

Other congressional actions have targeted the FDA's ability to regulate the pharmaceutical industry. In particular, the 1997 FDA Modernisation Act significantly improved pharmaceutical interests by requiring the agency to lower the standards for approving drugs 25 p.203. This involved accepting only one clinical trial for a drug instead of two and not requiring efficacy to be proven against an older drug already on the market or not using an inert placebo to observe harmful effects 25. When the pharmaceutical companies do not like something about the FDA they can change it by placing direct pressure on their 'friends' in Congress 25 p.10.

In 1980 two Acts were passed in Congress that enabled drug companies to license and profit from research that was supported by the National Institutes of Health (NIH) 25. This resulted in a rapid increase in the number of biomedical patents that were granted but there has been a lot of criticism about the consequences of this practice.

In 1992 Congress passed the Prescription Drug User Fee Act which gave pharmaceutical companies the directive to pay user fees to the FDA. The pharmaceutical companies had lobbied for this Act to speed up the approval process for drugs 25 p.208. Both the US FDA and the Australian TGA are funded by a user-pay system which makes them directly dependent on the industry they regulate for funding 25, 26. There is an inherent conflict of interest in selling drugs and assessing them. Does a business provide impartial advice on the products it sells? 25. The TGA is 100% funded by industry 26. Governments are 'pretending' that the advice they give on drugs and vaccines is impartial when clearly it is not 25.

The fees the industry pays for each new drug application are insignificant compared to the income generated by getting the drugs on the market rapidly. The majority of the fees are used

by the regulators to fast track approvals and only a small amount is used for limited safety monitoring 25 p. 208. Industry–paid employees represent more than half of the FDA staff involved in approving drugs (Krasner 2002 in 25). In the race to approve drugs the FDA is demanding less evidence of safety and efficacy of drugs and this is acceptable because the manufacturers of vaccines in the USA are exempt from liability if a product causes harm 23. Since 1992 thirteen prescription drugs have been withdrawn from the market after causing hundreds of deaths 25.

The Prescription Drug User Fee ensures that the agency has a direct interest in satisfying industry and this is what Congress expects 25 p. 210. Industry pressures are also apparent on the eighteen FDA advisory committees with many members having financial connections to interested companies 25. These factors all synchronise with an anti-regulatory administration to compromise the independence of the FDA and influence policy decisions 25 p.210.

Conflicts of Interest of Members of the Australian Technical and Advisory Group on Immunisation (ATAGI)

The ATAGI committee is responsible for providing immunisation advice to Australia’s Health Minister, Tanya Plibersek. The chairman of this committee is Professor Terry Nolan. In addition he is also the deputy chairman of the National Health and Medical Research Council (NHMRC): the body that controls the funding and direction of research projects.

Professor Terry Nolan’s conflicts of interests include being a member of a CSL vaccine advisory board (at some time) and receiving nominal payments (honoraria) as well as support for conference attendance from CSL Ltd, Novartis and GlaxoSmithKline 27. He was also the chief investigator of the clinical trial for CSL’s Panvax influenza vaccine in 400 children in 2009 27 even though he was also on the government’s primary advisory boards for policy-decision making at the time.

Professor Robert Booy is the co-director of the government National Centre for Immunisation Research and Surveillance (NCIRS). He is also a member of the government’s advisory committee on influenza – the Influenza Specialist Group (ISG) that is 100% funded by industry 29. Whilst holding these positions he was also an investigator in the clinical trial for children’s

Panvax (H1N1) influenza vaccine in 2009 which was funded by CSL 27. He has received support from CSL limited and other pharmaceutical companies to attend conferences. He has been a representative on a vaccine advisory board for these companies at various times and has also received funding from Roche, Sanofi, GlaxoSmithKline and Wyeth for attending and presenting at scientific meetings 27. These activities are a conflict of interest with his role as a government policy advisor and director of the government's research and surveillance unit yet they are not revealed to the public.

Associate Professor Peter Richmond is a member of the government's Influenza Specialist Group (ISG) (a body that is 100% industry funded) and also a member of ATAGI. At other times he has been a representative on a CSL vaccine advisory board 28. At various times he has received nominal payments from CSL (honoraria) and he was also an investigator in the CSL funded clinical trial for Panvax vaccine in 2009 27. He was influential in implementing the Western Australian Influenza Vaccine Efficacy trial (WAIVE) for children in WA (2008 – 2013) that was funded by CSL and Sanoffi –Pasteur (WA Health Dept. 2008). He stated in 2010 that 'I don't think investigators involved in clinical trials are working for CSL' 28.

Dr. Alan Hampson is the chairman of the Influenza Specialist Group (ISG) and he was previously the Research and Development Manager at CSL 30. He was instrumental in the formation and development of the ISG 29 and is a former deputy director of the World Health Organisation Collaborating Centre for Reference and Research on Influenza 29. He is also the Editor in Chief of the international journal *Influenza and other Respiratory Viruses* 29. He has a consultancy role with the WHO and the Australian Government 29.

Anne Kelso was a member of the ISG in 2010 and she had shares in CSL, Australia's only flu vaccine manufacturer. She was also in charge of the WHO influenza laboratory in Melbourne 31.

Judy Wilyman

PhD Candidate

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