CHAPTER 6

INDUSTRY INFLUENCE IN RESEARCH AND POLICY

6.1 Introduction

Cultural and political changes that have occurred since the mid-to late 20th century have resulted in government public health policies that have been increasingly influenced by corporate lobbying and sponsorship of research and education. The expansion of industry-sponsored university research during this time has led to a shift in the way knowledge is produced and published by academic institutions. There has been a decline in the autonomy over the production and transparency of academic knowledge. The commercialisation of scientific knowledge has changed the structure of academic institutions and this has been accompanied by a change in the traditional culture and values under which scientific knowledge is produced. The biggest area of commercialization in science has been in the biomedical and health sciences. In the era of globalisation research is being driven primarily for profit and not just for its contribution to knowledge.

This chapter describes the changes that have occurred to research institutions over the past fifty years and the way this has altered the culture and integrity of the scientific knowledge that is produced. I have provided specific information about the corporate influence in medical research from the US because this is where it is best documented but drugs are a global industry and these practices are occurring in (and affecting) many countries. The vaccine industry has expanded rapidly over the last two decades and regulatory processes have not kept pace with vaccine production. The effects of this rapid expansion on the regulatory processes for vaccines are described in this chapter. I have also described the conflicts of interest (COI) in medical research and policy development that can lead to a bias in the underlying science in the medical literature and in government public health policy. As there is no formal enforcement of values in medical research the public is dependent upon the honesty and integrity of the peer-review process to validate scientific knowledge. This chapter describes the influence of academic-industry partnerships on the peer-review process of scientific knowledge. Doctors are dependent upon their medical

education to make the best value judgments for their patients. To achieve healthy outcomes the information they receive should not be influenced by corporations that make a profit out of health interventions. I have described how industry sponsorship of the education of medical professionals influences the treatments that doctors provide to the community and also the direction of government public health policies.

This information is not a criticism of the involvement of industry in medical research per se or to suggest that capitalism cannot produce good science. It is to recognize that these influences can result in biased science and that transparency and patient autonomy in the use of all medical interventions are the key principles in maintaining healthy communities. The problems described in this chapter are still rife today even though it has been claimed that many of them have been addressed (Goldacre 2012 pxi).

6.2 The Academic-Industry Partnership

This section is informed especially by Marcia Angell because of her role as former chief-editor of the *New England Journal of Medicine* (NEJM) for 20 years. Her vast experience as the editor of this prestigious medical journal has led to many conclusions that are supported by other prominent authorities that are also cited in this section.

In the era of globalisation industry is providing funding for academic institutions, medical institutions and government bodies (Krimsky 2003; Angell 2005; Michaels 2008). The new image of a 'scientist' in the 21st century is the person who can make contributions to knowledge while participating in converting the new knowledge into a product for the market (Krimsky 2003 p1). This is termed *knowledge or technology transfer.* To facilitate technology transfer, university-industry partnerships have been established to direct research towards profit. In this new structure of academic institutions research ideas are patented by the industries that sponsor the research (Krimsky 2003 p30). Consequently it is possible for ambition and career success to bias the assessment of the research. This can erode the integrity of scientific institutions and eventually produces mistrust and scepticism in the general public (Krimsky 2003 p2). Partnerships with industry became common after the 1970's and 80's when universities needed to diversify their funding sources to remain

competitive. At this time there was an anti-regulatory atmosphere in the governments of many countries that facilitated the pathway to privatisation (WHO CSDH 2005). It became popular for universities to partner with the private sector and generate wealth by selling their knowledge and licensing discoveries (Krimsky 2003 pp28-9). The process of commercialising universities required changes to the laws. In the USA several congressional Acts, such as the Patent and Trademark Amendments Act (Bayh-Dole Act) and the Technology Innovation Act of 1980, were passed and tax incentives were provided by the government to encourage partnerships (Krimsky 2003 p30).

Many of the laws that were passed in the US Congress in the 1980's were designed to speed up the 'technology transfer' of government funded research into useful products. In particular, the Bayh-Dole Act granted patents to universities, small businesses and non-profit institutions from the research sponsored by the US National Institute of Health (NIH) (Angell 2005 p.202; Krimsky 2003 p30). This gave institutions title to the inventions made with federal research funds. It enabled exclusive licenses to be granted to drug companies for these patents. Prior to this Act, tax-payer funded research was in the public domain. Universities could subsequently patent and license their discoveries and also charge royalties (Angell 2005 p202). Sponsors can also own the clinical data, a practice that results in censorship of the medical literature (Goldacre 2012 p39). These political changes were a significant boost to the biotechnology and pharmaceutical industries and encouraged the establishment of many new biotechnology companies (Angell 2005 p202). It is now common for both academic researchers and their institutions to own equity in the biotechnology companies they are collaborating with. Therefore when a patent that is held by a university or a small biotechnology company is licensed to a drug company, the shareholders and employees will benefit financially from this publicly funded research. In medical schools prior to 1980 academic investigators who carried out industry-sponsored research rarely had conflicts of interest (COI) with their sponsors. However, since 1980 the medical schools themselves have a variety of deals with industry and are therefore not in a position to object to researchers behaving in the same way (Angell 2009). Conflicts of interest in industry funded research result in a systematic bias towards industry interests (Goldacre 2012 p38).

The Bayh-Dole Act transformed the ethos of medical schools and teaching hospitals to capitalize on research discoveries in medical schools. Many lucrative financial deals were established with drug companies in the 1990's and this has led to a significant 'pro-industry bias' in the medical research that is presented to governments for use in public health policies (Angell 2005 p202). This situation was demonstrated in a survey of medical schools in 2003 which showed that the majority held equity interest in companies that were sponsoring the research within the same medical institution (Angell 2009). An investigation of the department chairs also found that the majority received income from pharmaceutical companies for the department and most received personal income as well. Although medical schools were issuing guidelines in the 1980's about conflicts of interest they were variable, permissive and loosely enforced (Angell 2009). In the 21st century, there is not 'a single sector of academic medicine or medical education in which industry relationships are not ubiquitous' (Stamatakis et al 2013 p469).

The academic–industry partnership spread globally in the late 20th century and this has meant that pharmaceutical companies do not rely on their own research for new drugs. Consequently the production of prescription drugs tripled from 1980–2000. Prior to this, sales of drugs were static but the corporatization of medicine paved the way for the pharmaceutical industry to become the most profitable industry in America (Angell 2005 p203). The global pharmaceutical industry is a $600 billion industry 'rife with corruption and greed' (Goldacre 2012 p x). In 1980, the US Patent Act was altered to remove the requirement that patentable inventions should be 'novel, useful and non-obvious'. This change opened the door to acquiring patents for many more 'inventions' (Angell 2005 p176). The monopoly rights for brand-name drugs were further extended with the 1984 Hatch-Waxman Act. This meant that copies of the drug (generics) can only be placed on the market when the rights expire (Angell 2005 pp178-179). In addition, generic drugs do not require clinical trials to test for safety and efficacy before they are licensed by the FDA if they contain the same active ingredient as the brand name drug (Angell 2005 p179). Further, half the drugs approved in the US by the FDA from 2005-2011 were approved without companies having to demonstrate a measurable benefit of the drug (Downing et al

2014). The FDA did not require proof of the benefit of drugs that had innovative chemical structures, termed New Molecular Entities (NME). The risk-benefit profiles for drugs are not properly determined because active placebos, surrogate end-points and small sample sizes are being used in many clinical trials (Downing et al 2014).

The Act extending the monopoly rights on drugs through the US Patent and Trademark Office (USPTO) ensured that creating a monopoly and extending it for as long as possible was a very profitable activity (Angell 2005 p173). Industry could also increase its profits by obtaining exclusive marketing rights from the FDA. The monopoly rights for blockbuster drugs, those that earn over a billion dollars per year, such as the HPV vaccine, are golden for the pharmaceutical companies and can now extend for more than 20 years (Angell 2005 pp174-178). Pharmaceutical companies can extend this patent by licensing the drug for other diseases. Throughout the 1980's there was a rapid growth of US university-industry relationships particularly in the area of biotechnology. This type of sponsorship was 20% higher in biotechnology than any other sector and nearly 50% of biotechnology companies were sponsoring university research at this time (US Congress OTA 1988 in Krimsky 2003 pp31-32). During this decade at least 11 multimillion-dollar contracts for research in biotechnology were issued. Sponsorship by biotechnology companies in US universities reached $120 million by 1984. This figure represented 42% of all industry-sponsored university research (Krimsky 2003 pp31-32). This is relevant to vaccination policies because nascent biotechnology is being used to produce new vaccines for many communicable and non-communicable diseases and also new combination vaccines for childhood diseases.

6.3 The Influence of Industry Sponsorship on Medical Research

In the US and many other countries, university scientists play a crucial role in providing evidence for laws and policy. In the 21st century science is being produced with industry funding and goals which mean that 'expert' opinion can now be bought with a point of view (Michaels 2008 p47; Krimsky 2003; Angell 2005). Bias has affected the outcomes of all stages of the scientific process. This has significant consequences for policies and laws that are implemented in the public interest because these should be founded on a balanced

assessment of the body of research on a topic. The commercialisation of science has led to the pharmaceutical industry selling drugs to the community without performing properly designed randomised clinical trials (Kleinman 2005 p13; Angell 2009 pp109-114; Garrett 2012; Goldacre 2012 p2; Downing et al 2014). Industry-sponsored studies downplay the side-effects of drugs, with only the benefits being emphasised to doctors and the community (Stamatakis et al 2013 p470; Goldacre 2012 p2). This situation has been made possible because of the influence of industry funded sponsorship in research grants and clinical trials, and in medical education. Industry funds, designs and controls a large portion of the most influential medical research and education (Stamatakis et al 2013 p470).

There is increasing direct evidence of the manipulation of results in industry funded trials (Stamatakis et al 2013 p470; Goldacre 2012 p21). Ioannidis (2005) concluded that nearly half of published articles in scientific journals contained findings that could not be replicated by independent researchers. In fact, he showed that most research findings are false. This problem is noted to be particularly widespread in medical journals where peer-reviewed articles can be crucial in influencing multi-million dollar spending decisions. Conflicts of interest in these journals compromise the neutrality of published research (Epstein 2011; Angell 2005; Krimsky 2003). Drug companies can select which clinical trials they will publish and the suppression of trials with negative results is producing medical literature with false positive findings (Goldacre 2012 p2). In biomedical research, COI are very common but they are rarely reported (Ioannidis 2005). The bias can be financial or just a commitment to their own findings (Ioannidis 2005; Goldacre 2012). It is observed that the peer-review process can be used by prestigious researchers to suppress the publication of findings that refute their research (Krimsky 2003 p10; Ioannidis 2005; Michaels 2008; Angell 2005). This results in the perpetuation of false claims. Ioannidis (2005) states that the more popular the scientific field, the less likely the research findings are to be true.

Medical journals are involved in COI because 50% of their income is derived from pharmaceutical advertising and reprint orders (Angell 2009). Many journals are also owned by companies who operate as medical publishers but in effect provide a marketing service

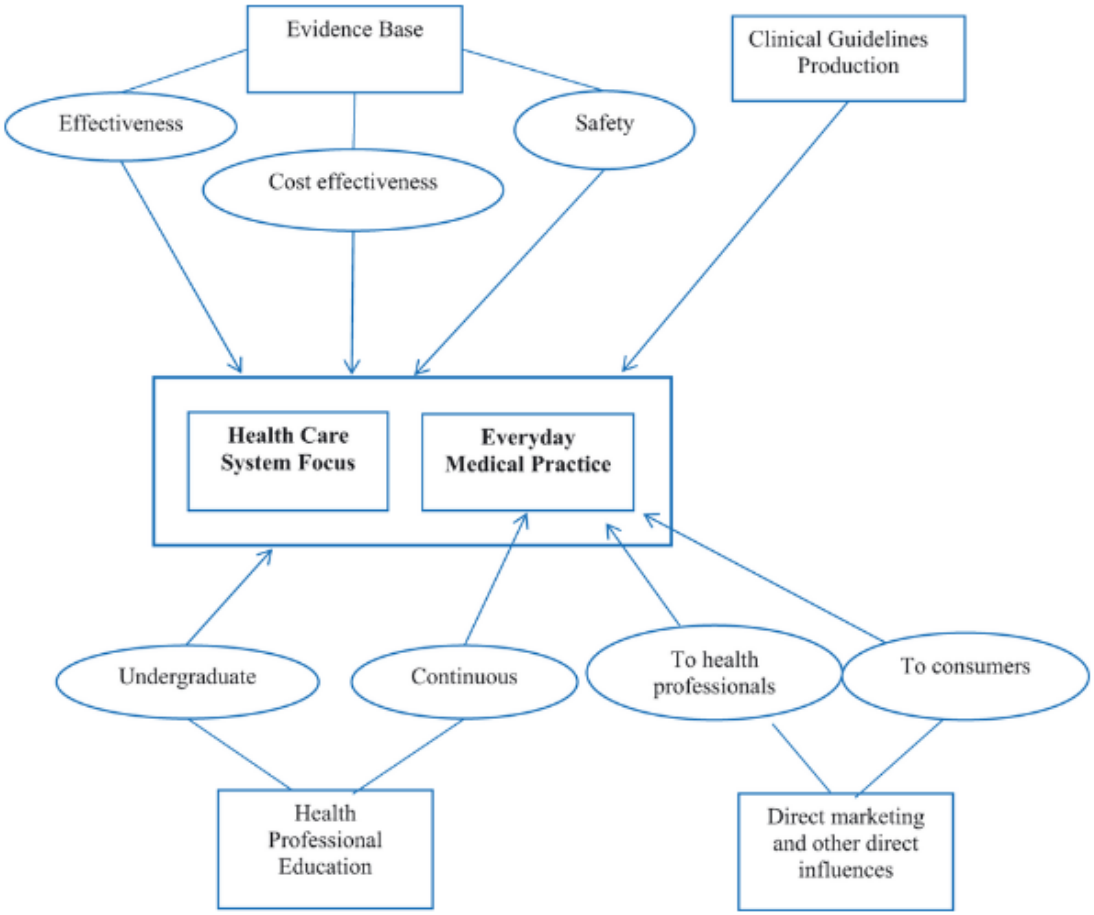
to the pharmaceutical industry (Angell 2009; Goldacre 2012 p38). Another COI in published studies is the financial ties many authors now have with the companies that sponsor their research. In the 1990's the decline in US government funding for medical research left medical scientists dependent on pharmaceutical companies to fund their work (Bosely 2002). Sponsors continue to control the data even when lead authors declare that researchers had full control over publishing decisions (Goldacre 2012 p41). Industry has gained unprecedented control over trial data and this has increased the opportunities for company employees to draft research papers and it has led to the practice of 'ghostwriting' and 'honorary authorship' (Bosely 2002).

The practice of ghostwriting is very common in the commercialised era of science (Krimsky 2003 p115; Peterson 2008; Seife 2012). This practice involves doctors being paid to put their names on a paper they haven't written. In this way credibility due to apparent independence is conferred on the findings of industry funded research. It is a deceptive practice akin to plagiarism that has become common in the marketing of scientific and medical research (Krimsky 2003 pp115-117). Many pharmaceutical companies now market drugs through a PR firm that hires a freelance writer to write an article and a doctor to put their name on it (Krimsky 2003 p116). The doctor can be paid $1,000-$10,000 for their contribution (Bosely 2002). It is then presented for publication in a peer-reviewed journal. Industry can also influence which research is published in the most influential medical journals by using ghostwriters (Stamatakis 2013 p471). The status of industry trial results can be raised by listing academically affiliated investigators as the first or second authors of the articles (Stamatakis 2013 p471). This has been done for publications regarding the HPV vaccine and is described in Chapter 10. This practice is deceptive to researchers and consumers and should be considered scientific fraud. However, much of the medical community has accepted the practice and participates in it for the financial rewards (Krimsky 2003 p115). It is also a hidden practice. In many cases, it is alleged that the authors will not have seen the raw data they are writing about – only tables of data prepared by industry employees (Bosely 2002). Originally ghostwriting was only found in medical journal supplements sponsored by industry but it is now widespread in all the major journals (Bosely 2002).

Ghostwriting or honorary authorships erode the integrity of science. Doctors are also presenting talks on ghostwritten papers at drug-company sponsored symposiums and receiving money for the talk, airfares and accommodation (Bosely 2002; Angell 2005; Peterson 2008). To combat the ghostwriting of articles, the editors of medical journals claimed they would introduce a system requiring scientists to sign a declaration that the papers they submitted to peer-reviewed journals were their own work. However, the practice of ghostwriting continued (Seife 2012). Many journals have also denounced drug companies for restricting the access of scientists to the raw data of clinical trials (Stamatakis 2013 p471; Bosely 2002). In addition, it is known that drug companies do not publish trials with negative findings. Researchers can do many trials but they are free to choose which ones they will publish (Goldacre 2012 p7). This results in 'publication bias' and it is endemic in medical and academic institutions. Regulators have failed to address this problem. Incomplete data on the safety and efficacy of drugs in the medical literature misleads doctors, patients and policy-advisors resulting in harmful decisions in patients (Goldacre 2012 p27). Dr. Richard Horton, chief editor of the *Lancet*, stated at a symposium on biomedical research at the Wellcome Trust in London that half of the scientific literature is unreliable and much is fraudulent (Engdhl 2015). He says pharmaceutical companies are manipulating the tests on the safety and efficacy of drugs/vaccines and these studies are being used to train and educate doctors: COI, lack of transparency, invalid analyses and the funding of fashionable trends, such as innovative biotechnologies, are facilitating this situation.

The integrity of health promotion organisations is threatened by the influence of industry sponsorship (Krimsky 2003 p79). Sponsors fund and influence all aspects of research, evidence synthesis, cost-effectiveness evaluation, formation of clinical guidelines, conferences, grants, healthcare professional education and healthcare professional decisions (Stamatakis 2013 p471). These pathways for influencing medical practice and healthcare are illustrated in Figure 8.

Figure 8 An outline of the main pathways through which the industry influences medical practice and the focus of the healthcare systems.



Source: Stamatikis E, Weiler R, Ioannidis J. 2013. Undue industry influences that distort healthcare research, strategy, expenditure and practice: a review. *European Journal of Clinical Investigation.* May. 43: 5: p470.

Financial involvement in these areas provides an opportunity for industry to influence every aspect of medical institutions. But the areas of most significance are the sponsorship of doctor's education and the direction of research (Krimsky 2003 p31). These directly impact on the ability of doctors and scientists to protect the public interest. Doctors and scientists now participate in the following activities that represent a conflict of interest to their professional guidelines (Angell 2005):

- consult for companies whose products they are researching

- join company and government advisory boards
- become members of speakers bureaus for drug companies
- have patent and royalty arrangements
- agree to be listed as authors of articles ghost written by interested companies
- promote drugs and devices at company-sponsored symposiums
- accept expensive gifts and trips
- have equity interest in the companies sponsoring the research

Examples of these practices are illustrated in the case study of the HPV vaccine in chapter 9. Many research institutions and medical bodies receive large amounts of money from pharmaceutical and biotechnology companies that the public is not made aware of. Exact amounts of sponsorship are unknown to the public (Krimsky 2003). Industry funding can aid the development and progression of science but it is imperative that industry partnerships are managed in a transparent process. This is necessary to maintain the integrity of the scientific/medical profession and ultimately the authority of medical doctors in the community (Stamatakis 2013 p.473; Goldacre 2012 p45). Integrity, objectivity and independence are central to the translation of evidence-based knowledge into clinical guidelines (Stamatakis 2013 p471). It is now common in the medical field for doctors to receive money or gifts from drug companies (Krimsky 2003; Angell 2005 p115; Peterson 2008). This includes funding for conference travel, accommodation, shares, consultancy fees, honoraria for speeches in drug promoting events and other products (Stamatakis 2013 p471). Between 56-87% of the authors for clinical practice guidelines have at least one conflict of interest (Norris et al 2011). Research in social psychology suggests that large gifts to doctors can influence behaviour and small gifts can influence attitudes towards the company and its products (Krimsky 2003 p33).

Research on the influence of gifts to doctors was used by a subcommittee in Congress in the 1990's to recommend against COI in drug evaluations. The committee requested that the Department of Health and Human Services (DHHS) 'immediately promulgate Public Health Service regulations that clearly restrict financial ties for researchers who conduct evaluations of a product or treatment, in which they may have a vested interest' (Krimsky

2003 p33). However, this request was never acted upon (Krimsky 2003 p33). The boundary between industry and academia has become blurred and clinical guidelines are now founded on costly interventions instead of the available evidence (Stamatakis 2013 p472). The bias in clinical research is enhanced when financial incentives are provided to doctors or policy advisors (Krimsky 2003 p7). Drug companies subsidise the majority of meetings of professional organizations thereby influencing the content of these meetings. In addition, they fund the continuing education of doctors to maintain their licenses (Angell 2005 p135). This enables the drug companies to influence doctors' views about drugs. Side-effects can be down played and benefits enhanced when the drugs/vaccines are promoted at industry funded conferences (Stamatakis 2013 p472; Angell 2009; Goldacre 2012). Consequently, in an unregulated environment, the health advice provided to consumers is strongly biased towards industry priorities (Stamatakis 2013; Goldacre 2012). Angell (2009) estimates that drug companies pay US physicians tens of billions of dollars a year which gives them enormous control over the way in which doctors practice. In particular, they have control over the way doctors evaluate and use pharmaceuticals. Drug companies have significant influence over the results of research, the way medicine is practiced and the definition of what constitutes a disease (Angell 2009; Stamatakis 2013). This is all possible because of the financial ties they have to doctors and in particular, senior academics at prestigious medical schools (Angell 2005 pp142-147). It has also been demonstrated beyond doubt that studies funded by industry produce positive results more often than independently funded studies (Goldacre 2012 p1). This is called the funding effect.

In order to carry out clinical trials, drug companies need access to human subjects therefore many of these trials occur in medical schools to provide access to hospitals. Alternatively they are done through private research companies. By utilizing the medical schools for clinical trials the drug companies can work with highly influential academic physicians (Angell 2005 p142). These doctors are referred to as 'thought-leaders' or 'key opinion leaders' (Angell 2005 pp142-147; Peterson 2008). Many of these doctors write text books, medical journal papers, issue practice guidelines (treatment recommendations), sit on the FDA and government advisory committees, head professorial societies and speak at many

conferences for clinicians about prescription drugs. Access and gifts to these physicians benefit pharmaceutical companies and provide many opportunities to influence medical practices (Krimsky 2003). The growing number of scandals in which the dangers of prescribed drugs have been discovered too late led a group of scientists and clinicians to write an open letter to the UK Prime Minister (Archibald et al 2011). The letter stated that adverse drug reactions have reached epidemic proportions and are increasing at twice the rate of prescriptions. This leads to the question of whether drugs/vaccines are being adequately trialed and tested for adverse reactions before being approved by boards dominated by individuals affiliated with industry (Stamatakis 2013 p471). Data from a litigation trial against a pharmaceutical company suggested the manufacturer intentionally altered the presentation of trial safety data and trained sales representatives to avoid questions from doctors about safety (Stamatakis 2013 p471). Goldacre (2012) states that manufacturers test drugs in poorly designed trials that use analytic techniques that exaggerate the benefits and downplay the risks and they do not publish trials that represent the body of scientific data on a topic (p21).

The harmful effects of drugs are being minimised by choosing incorrect parameters and selective criteria in the design of clinical trials. Primary data that is not independently assessed by the scientific community can be massaged to produce the desired result through the choice of methodology and criteria (Michaels 2008 p53; Goldacre 2012 p2). The sponsor of the trial can then claim ‘there is no evidence of harm’ simply because the study did not use the parameters that might have revealed harm from the drug/vaccine. This is biased or misleading science and it is being used in public health policies. In the new structure of university funding and governance the available evidence can be influenced at all stages by the sponsor to prevent vital evidence from being collected.

6.4 Australian Examples of Academic-Industry Partnerships

An example of the academic-industry partnership in Australia is found at Murdoch University, which has recently collaborated with many corporate partners to form the Institute for Immunology and Infectious Diseases. This is an international medical centre

with over 30 collaborations and significant international funding, including $12 million from the Bill and Melinda Gates Foundation. Other partners include the Royal Perth Hospital, Fiona Stanley Hospital, biotechnology industries, Microsoft Corporation, GlaxoSmithKline, Merck, Roche and other pharmaceutical industries. The research program at the new medical institute is titled 'The Genesiis Campaign'. This is in reference to a new era in the fight against infectious diseases based upon recent research in the understanding of human genetics and differences in individual gene patterns. The institute aims to open the door to new treatments and vaccines for infectious diseases. Its goal is to be a top international multidisciplinary research centre focusing on contemporary issues such as AIDS research and clinical and diagnostic care. In achieving this goal, intellectual property and commercial benefits will be secured to Western Australia. In 2011 there were two patents being developed in the international phase (Murdoch University 2011).

Another Australian example of academic-industry collaboration is the University of Queensland (UQ) and CSL Ltd (Uniquest). UQ collaborates with Uniquest Pty Ltd, a company that manages the university's commercial interests such as the sale of products that are based upon UQ technology. According to Uniquest, innovations that it has licensed have sales of $3 billion per year, putting it in the top 10% of universities worldwide for technology transfer (Uniquest). This partnership is described further in chapter 9.

6.5 The Global Regulation of Vaccines

In the era of globalisation many pharmaceutical products such as medicines and vaccines are no longer being produced and regulated in the countries in which they are used. As a result there is now a vast international network of production and distribution. However, the industry has expanded rapidly and the distribution problems are resulting in sub-standard vaccines. The increased demand has resulted in criminal, false products in some cases (Garrett 2012b). There is concern that the regulatory processes are not keeping up with changes in the industry and it is alleged that organised crime is increasingly involved in the production of medicines. Regulators are over-whelmed or non-existent in many countries. The WHO does not have the legal framework to effectively address these

problems so the Council on Foreign Relations (CFR) is looking to the G8 and G20 countries for solutions (Garrett CFR 2012).

Government regulators of drugs/vaccines for many countries are funded by the industry whose products they approve (Goldacre 2012 p128). This includes the European Medicines Agency (EMA), the Medicines and Healthcare products Regulatory Agency (MHRA) (UK regulatory board), the US Food and Drug Administration (FDA) and the Australian Therapeutic Goods Administration (TGA). The situation where government regulators promote the interests of the industries they monitor instead of the public interest is described by sociologists as 'regulatory capture'. This is now a global practice even when regulatory boards state 'members of the Management Board shall not have financial or other interests in the pharmaceutical industry which could affect their impartiality' (Goldacre 2012 p126). Despite this requirement many of the representatives on EMA boards come from pharmaceutically funded companies, including on their management board. It is observed that regulatory decisions in the US FDA have been influenced by political pressure because of this practice. The FDA has even been described as an 'agent of industry' to the US Senate Committee on Finance (Goldacre 2012 pp127-8). Dr. Lucija Tomljenovic, at the University of British Columbia's Neural Dynamics Research Group in the Department of Ophthalmology and Visual Sciences, has been quoted as saying 'vaccine manufacturers, pharmaceutical companies and health authorities have known about multiple dangers associated with vaccines but chose to withhold them from the public. This is scientific fraud and their complicity suggests that this practice continues to this day' (Enghahl 2015).

6.6 Conflicts of Interest in the Regulation of Vaccines in Australia

The information provided in this section regarding the Australian Therapeutic Goods Administration (TGA) has been largely sourced from the Australian government's website and a WHO review of the functioning of advisory boards for vaccines funded by the Bill and Melinda Gates Foundation.

The Therapeutic Goods Administration (TGA) was established in 1989 and it is the Australian government regulator of therapeutic goods such as medicines, vaccines and

blood products. This board, like the vaccine regulatory bodies in governments globally, is conflicted by being 100% funded by the industry whose products it monitors (AG RWAR 2010 p10). This funding system is known as Cost Recovery (or User-Pay) and it means that the TGA recovers the full cost of its regulatory activities by charging the sponsors and manufacturers of the products that are regulated. The pharmaceutical and manufacturing industry funds the TGA even though this government board has the dual role of approving drugs for its sponsor and monitoring the safety of these same drugs in the Australian population (AG TGA 2012). In order to effectively regulate in the public interest the TGA would need to be independent from industry funding. Regulations that provide incentives for producing *profit* and not *health* in government policies, compromise all participants in health promotion – doctors, researchers and policy advisors. These regulations encourage individuals – even those with integrity - to participate in decisions that cause significant harm to patients and the community (Goldacre 2012 pxi).

The activities of the TGA in the cost-recovery program include:

- Registration and approval of drugs/vaccines
- Issuing exclusive rights, licenses and privileges
- Monitoring ongoing compliance with regulations
- Monitoring ongoing safety of the products
- Investigation and enforcement of regulations

At present the processes of the TGA are not transparent to the public and funding arrangements for this government body illustrates that pharmaceutical companies are influencing the approval and monitoring of drugs/vaccines in the population. In addition, consumers whose health is invested in these policies are not properly represented in the decision-making processes of the TGA or on vaccine advisory boards for public health policy. The fact that the TGA is funded by the pharmaceutical companies and manufacturers of medical devices creates an incentive for bias towards industry interests. Funding arrangements and COI for committees that control the health of the population should be transparent to the public. The TGA justifies the COI in funding arrangements and policy decisions by suggesting that ‘it requires commercial companies that apply for

marketing approval to pay for the cost of the review of the application on a cost recovery basis' (AG RWAR p10). But this arrangement does not explain why the TGA has the responsibility for monitoring the safety of these products in the population when their procedures can be influenced by the industry that manufactures the product and sponsors the TGA. A regulatory body, to protect the public interest, needs to be independent of commercial interests (Gessner et al 2010 A4). The current funding situation for the TGA does not provide incentive to implement an effective monitoring system for vaccines because the TGA is monitoring the very drugs it has approved for its sponsors for commercial gain. Whilst the TGA states that it rigorously enforces conflict of interest requirements there is no evidence of this and up to 2015 the conflicts of interest of members of vaccine advisory boards have not been disclosed to the Australian public. The clinical trials used by government regulators to approve drugs are being funded by industry and performed by researchers who are voting members on vaccine advisory boards for the Australian government (Nolan et al 2010).

The Influenza Specialist Group (ISG) that provides advice on influenza policy in Australia is also fully funded by industry (Sweet 2011). The ISG justifies this situation by claiming that 'they (the ISG) are helping promote public health messages, not pushing specific brands of vaccine' (Finch and Burson-Marsteller in Sweet 2011). However, this does not justify the position of the ISG because the committee makes decisions affecting the financial interests of industry, specifically whether a vaccine is used as a preventative strategy against influenza: a multi-million dollar decision. The consequences of this decision make a significant difference to the profits of vaccine manufacturers. Therefore, it is essential that this public health decision is determined independently of the manufacturers. Whilst the existence of a conflict of interest does not automatically lead to bias it is important they are made transparent to the public if they are allowed to exist in the decision-making process. This allows consumers to judge the value of the information they are receiving, particularly when decisions are made that are contrary to the evidence. If boards are not truly independent of commercial interests the health information can potentially be influenced by these interests and COI need to be transparent to the public. Value judgments made in political decisions can have serious implications for public health. In 2008 at least two members of the ISG believed that the advice given by the ISG

regarding influenza policy was questionable. Associate Professor Michael Whitby, an infectious disease physician, decided not to be actively involved on the ISG committee because:

'He was concerned about the organization promoting influenza vaccination for indications not supported by national guidelines, especially the promotion of vaccination of children' (Sweet 2011).

Professor Peter Collignon and colleagues expressed similar sentiments in an article that was published in the *British Medical Journal* (Collignon et al 2010). Collignon has also been quoted saying 'The TGA made that decision (about risk-benefit to children) without any evidence to back it up' (Corduroy 2010). At this time there were members of the ISG that had financial COI that had not been disclosed to the public. One member of the Influenza Specialist Group (ISG) had been the previous Research and Development Manager at Commonwealth Serum Laboratories (CSL), Australia's only flu vaccine manufacturer (Dean 2009). Another member had shares in CSL and was in charge of the WHO influenza laboratory in Melbourne at the time the 'Swine Flu' pandemic unfolded (Bita 2011). The Australian government states that committee members are required to declare any conflict of interest and this is 'taken into consideration at meetings' (Bita 2010). If these conflicts of interest are unavoidable then it is important that they are made transparent to the public because it is known that financial connections can affect policy decisions. This information is needed by the public to make informed decisions about their health otherwise they are left to *trust* that government decisions are in the public's best interest. Some public health experts have called for an independent body to monitor drug safety because it is clear that self-regulation of the industry is not in the public interest (Stokes 2010; Baxter 2010; Moore in Corderoy 2010).

6.7 Conflicts of Interest in Government Vaccine Advisory Groups (ATAGI)

A sustainable vaccination program recommending many new vaccines, most of them free, cannot be provided to Australians without an effective funding mechanism. The cost of Australia's vaccination program by 2008-2009 was well above $AU400 million (Nolan

2010 A76). During 1990-1997 the recommendations for the funding of vaccines in Australia were made by a sub-committee of the NHMRC. This committee was also responsible for developing the *Australian Immunisation Handbook*: a government document outlining national clinical guidelines for all health professionals. The governance of this sub-committee was brought under government control in 1997 when it was moved into the Department of Health and Ageing (DHA). At this time the board was re-named the Australian Technical Advisory Group on Immunisation (ATAGI) and its main roles were to provide confidential advice to the Health Minister and to develop guidelines for health professionals in the *Australian Immunisation Handbook* (Nolan 2010 A76-77). In producing the guidelines for health professionals in Australia, ATAGI is required to adhere to the NHMRC's guidelines for the levels of evidence and ethical behaviour in healthcare and medical research.

ATAGI is an example of the many National Immunisation Technical Advisory Groups (NITAG) that have been set up with the assistance of WHO, in member countries, to develop government vaccination programs founded on WHO recommendations (Bryson et al 2010 A13). See chapter 3. These boards provide information for the government to make decisions regarding recommendations on vaccination schedules and the implementation of new vaccines. They also provide advice on research priorities, vaccine formulations, high-risk groups and the implications of adverse events (Gessner et al 2010 A2). Representatives on ATAGI include medical and public health practitioners, technical experts, ex-officio members (government bodies e.g. NCIRS, OHP, TGA, NIC, CDNA) and one consumer representative (AG IAP 2012). In fact, WHO has stated that the inclusion of a civil/public representative is optional and only 'if needed' (WHO ITAG 2008 p5). This contradicts the statement that these boards are 'independent' and representative of all stakeholder interests. Australian government vaccination policies are developed on the advice provided by these expert technical advisors who are selected to ATAGI by the Health Minister through an informal nomination process (Nolan 2010 A79). Given that vaccine advisory boards include experts associated with industry, the boards should also include representatives of the public. This is because the public is the stated beneficiary of public health policies: the major stakeholder. If a major stakeholder is not properly represented in policy development then their perspective of risk can be minimised in policy decisions. In this way, a one-sided

consensus can be achieved when there is insufficient dissent to oppose the dominant interests on the advisory board. A stakeholder's perspective can be further side-lined if they are not properly represented in the media, in the political domain or involved in public debates on the topic. A lack of balance in the media removes the stakeholder's voice from the debate and synchronises with a lack of political power. When there is only one representative of a stakeholder on the advisory panel I believe it is also possible to choose a representative who is in agreement with the desired perspective and/or influence their opinion by ensuring they gain financially from their participation. It is possible for policy decisions to be founded on biased or 'selected' information when specific political structures such as COI exist. See chapter 8.

In Australia members of ATAGI hold their positions for many years. The term is set for 4 years but can be extended at the Minister's discretion (Nolan 2010 A79). For example, Terry Nolan was the chair of ATAGI for 9 years from 2005-2014, Peter McIntyre (2004-2015) and Robert Booy (2005-2015), co-directors of the National Centre for Immunisation Research and Surveillance (NCIRS), have been members/ex officio members of ATAGI during this time (AG NCIRSn). Conflicts of interest are a concern on the ATAGI board because the decisions made have significant implications for vaccine sales for pharmaceutical companies. It is stipulated that committee members of ATAGI must be independent of pharmaceutical industry influence (Gessner et al 2010 A3) and the Australian regulations state that a detailed agenda is sent to each representative before each meeting to update relevant COI (Nolan 2010 A79). However, declaring a COI does not remove it and it is the public that needs to be informed of these relationships to protect their interests in these policies. COI on the ATAGI board were not publicised prior to 2015. The COI policy for ATAGI members has variable consequences that are determined by the chair of ATAGI in consultation with the chair of the PBAC and other government members (Nolan 2010 A79). Depending on the level of COI, members can participate and vote, participate and not vote, attend meetings but not contribute or be prevented from attending meetings altogether (Gessner et al 2010 A3). The chair's own COI and decisions about the consequences of COI are not transparent to the public. It is stated that in general 'personal remuneration of other forms of direct or indirect financial or other benefits for marketing or promotional activities are inconsistent with ATAGI membership' (Nolan 2010 A79). Over

the last decade, 2005-20014 many ATAGI representatives had COI with vaccine manufacturers that were not revealed to the public. During this time many new vaccines were added to the recommended schedule of vaccines that are paid for by the government and provided free to the community.

The chair of ATAGI from 2005-2014 was also the deputy chair of the research committee of the National Health and Medical Research Council (NHMRC): the committee that allocates funding for research projects (DHA 2012). Nolan states that involvement in industry-sponsored vaccine research is generally not considered a conflict of interest that requires exclusion if the payment is made to the institution and not the individual (2010 A79). However, industry grants for vaccine trials are not provided to institutions to allocate to projects of their choice. They are usually provided to specific researchers for specific vaccine trials. Over the last decade many members of ATAGI, including the chair and co-directors of NCIRS, have been chief investigators on vaccine trials that are funded by GlaxoSmithKline, Merck, Pfizor, Novartis, Sanofi, BioCSL, Baxter, Wyeth, Merck, Janssen &Janssen (Crucell) (AG ATAGI 2015; Nolan et al 2010). Many members have also been representatives of vaccine advisory boards at some time and received individual payments (honoraria) from vaccine manufacturers for their attendance at conferences (Nolan et al 2010). In addition, there is no funding provided by the NHMRC for vaccine clinical trials or research that is independent of vaccine manufacturers.

NITAG's, such as ATAGI, are described as consisting of independent experts with the technical capacity to evaluate new and existing immunisation interventions. The premise of these groups is to provide a systematic, transparent process for developing immunisation policies by making 'evidence-based technical recommendations' to the national government (WHO ITAG 2008). Their role is described as being 'technical' and 'advisory' and it is intended to bring 'increased scientific rigour and credibility to the complex process of making immunisation policies, free of political or personal interests' (Bryson et al 2010 A13). Yet it is clear from the governance of Australia's vaccination policy that vaccine advisory boards such as ATAGI are not using a systematic framework of assessment or evidence from the local community and they are not independent from vaccine manufacturers, government influence or transparent in their processes and assumptions. See

chapter 4. Bryson et al state that the credibility of NITAG's relies on 'true independence from the government' (2010 A16) yet ATAGI is heavily influenced by government representatives from NCIRS, NIC, PBAC, OHP.

There is global concern about the significant influence of government in NITAG committees and the lack of independence from political interference (Gessner et al 2010 A4). Gessner et al (2010 A4) state that scientific information from pharmaceutical companies should be presented through documents or via telephone and not through industry representation and participation in NITAG meetings. This is particularly the case as the public is not invited to attend these meetings or to present information to the committee. The US Government justifies the use of expert panels by claiming it cannot assemble, from its own staff, the expert knowledge necessary to address the diversity of technical issues under the government's responsibility (Krimsky 2003 p92). Hence the government suggests that it is broadening the knowledge base that is used in the decision-making process by using external expert advice. A government report even stated 'Advisory committees continue to represent part of federal efforts to increase public participation' (US Government Report in Krimsky 2003 p92). For decades university staff and academics have been encouraged to work with industry in equity arrangements. Therefore regulations prohibiting experts with COI from participating in policy decisions would remove many well qualified people from the assessment process and it would also be hard to find experts without COI. Hence this regulation is difficult to enforce (Goldacre 2012 p128). This indicates that the solution lies in having a decision-making board that has transparent COI and has proper public representation and scrutiny, without financial ties to industry or government influence.

6.8 The Approval Process and Funding for Vaccines

ATAGI consults with other government advisory boards and it provides advice to the government's pharmaceutical benefits scheme (PBS) on the strength of evidence for the funding of new vaccines. One member of ATAGI doubles as a member of the pharmaceutical benefits advisory committee (PBAC) (Nolan 2010 A79). The government

funded National Centre for Immunisation Research and Surveillance (NCIRS) also plays a significant role in the advice provided by ATAGI and in setting up working parties. (Nolan 2010 A79). See Appendix 4. Recommendations for the funding of vaccines made by the PBAC to the health minister are based on the manufacturer's submission and ATAGI/ NCIRS advice. Whilst pharmaceutical companies do not have formal representation or voting rights on the NITAG committees, industry representatives are allowed to attend meetings and provide information yet in Australia these meetings are not open to the public to attend or to present information (Gessner et al 2010). There is no transparency in who has been allowed to provide 'factual' information or to participate in decisions at ATAGI meetings.

ATAGI does not use a systematic process for collating and assessing data for the decision-making process. Some criteria used in making recommendations include the mortality and disability data attributed to the disease but not always local mortality or disability data. Other data that is used is disability-adjusted life years lost (DALY), hospitalizations, epidemic potential and the potential for disease eradication. Local data is relevant for all infectious diseases and also for the outcomes for vaccines in different populations but this is not always used in the economic modeling for new vaccines in many countries (Gessner et al 2010 A3). Decisions regarding the inclusion of a new vaccine on the Australian NIP are determined by an ATAGI sub-committee ahead of the licensure of the vaccine. Nolan states that considerations for the suitability of a new vaccine include the implications for herd immunity but this (herd immunity) is 'neither necessary nor sufficient for a positive recommendation for NIP suitability' (Nolan 2010 A79). This is of note because the government is using claims about vaccine-created herd immunity to justify its use of coercion to promote vaccination.

Data that is used to develop recommendations is sourced from WHO documents, journals, other NITAC's and regional/ local sources. The final decisions made by NITAG committee's for national programs are often influenced by WHO recommendations. Most committees adopt all of the WHO recommendations and some adopt them with modifications to local priorities. Whilst the recommendations made by the committee are only advisory and not legally binding, Australian health ministers depend upon ATAGI

advice. Nolan (2010 A81) stated that the assumptions and economic principles underpinning the recommendation process were still being debated but that they were widely accepted by industry and healthcare professionals. There is no mention that they have been examined or accepted by consumers. All ATAGI working parties are chaired by an ATAGI member and supported by one or more scientific officers from the NCIRS who are responsible for writing the report (Nolan 2010 A82). Nolan states that the policy branch of the NCIRS is critical to the quality of the advice provided to the government and health professionals.

Since 2005 funding applications for new vaccines have been addressed by a sub-committee of the PBAC, not by ATAGI (Nolan 2010 A79). The methodology for determining the cost-effectiveness and funding for vaccines is based on price per disability-adjusted life year (DALY) saved (Nolan 2010 A78). The cost-effectiveness of vaccines is determined by examining the evidence of the benefit of the vaccine from large clinical trials. This can then be used to estimate the cost of saving one quality-adjusted life year (QALY) which translates to the number of doses that need to be given at the vaccine cost to gain one extra year of full quality life (McIntyre 2012). This economic modeling, which relies on many non-transparent assumptions about the effectiveness and safety of vaccines, has resulted in the recommendation of many new vaccines into the Australian population since the 1990's. Unlike the UK there are no specific cost-effectiveness cut-offs for making recommendations for vaccines in the Australian NIP (Gessner et al 2010 A3). It is also of note that the price of vaccines funded by the Australian government is not made available to the public even on request (AG DHA 2013).

The recommendations for vaccine funding are included in the PBAC framework for all drugs marketed in Australia. The PBAC receives submissions mostly from pharmaceutical companies on the cost-effectiveness of new vaccines/drugs. Vaccine sponsors may request that a vaccine be recommended on the NIP, and subsidized by the government, or listed on the PBS where a co-payment is required from consumers (Nolan 2010 A82). The general criteria for vaccines to be recommended on the NIP are defined in the *Vaccine Appendix* of the PBAC submission framework which has been developed with significant influence from the Medicines Australia Vaccine Industry Group (MAVIG), a sub-committee of

Medicines Australia that represents the pharmaceutical companies. Whilst the ATAGI recommendations are founded on input received from many different professional, industry and government groups, the general public does not actively participate in ATAGI discussions and ATAGI does not conduct open forums for debate (Nolan 2010 A82). In addition, the unabridged ATAGI working party reports on vaccine recommendations are not made public. This is stated to be because they contain unpublished clinical trials that have restrictions on releasing the data. If this is the case it also means that the material has not been peer-reviewed by independent scientists and its integrity is questionable. Public health is at risk if the scientific data cannot be viewed and debated by all stakeholders before new vaccines/drugs are approved in government public health policies. The existence of COI on decision-making boards and the use of non-transparent science facilitate policies that can be developed on selective science of questionable integrity chosen by the dominant network of scientists. See chapter 8.

6.9 Conclusion

In the 21st century universities and research institutions are operating in partnerships with industry and directing research into profitable technology. Universities receive large amounts of money from industry that are not transparent to the public. COI are ubiquitous in financial relationships involving researchers in university faculties. Consequently industry has unprecedented influence over the type of research that is performed and the outcomes achieved. COI also exist in relationships involving the medical profession, media and government. These relationships play a significant role in the way drugs/vaccines are promoted to the community. When industry funds the research it leads to less public interest science being investigated because it might not serve industry interests. This is termed ‘undone science’ and the political framework for this practice is described in chapter 8. Vaccines/drugs are being approved for the market without properly designed clinical trials. The side-effects of drugs are being down-played to doctors and consumers and the benefits are over-emphasised. Many peer-review journals now depend upon industry funding for their profits and this increases the publication bias towards positive trial results and the suppression of negative results. Pharmaceutical companies are also sponsoring lobby groups that appear to be advocating for consumer interests but in fact are

fronts for drug companies. This influence synchronises with pharmaceutical marketing to doctors which is presented as 'education' and the media promotion of vaccines influenced by corporations. Consequently there is a systematic bias towards industry interests in medical research and public health policy and promotion.

A lack of acknowledgment by governments of an important area of research is easier to maintain if the stakeholder whose interests are affected is removed from the political decision-making process. This is observed in the development of Australia's vaccination policies as the community is not consulted or encouraged to participate in public debate on vaccination and there is only one consumer representative on the government vaccine advisory committee (ATAGI). In addition, pharmaceutical representatives can be invited to ATAGI committee meetings to provide information but these meetings are not open to the public and the information is not available for public scrutiny before vaccines are approved. A lack of political power and financial support also has the effect of reducing the consumer voice in the mainstream media. These factors are synchronising to remove an independent consumer perspective from the risk assessment process of policy development. They are also resulting in non-transparent policy decisions being made by ATAGI/NCIRS members in an unsystematic assessment of the risks.

The lack of independent regulation of the global vaccine market is resulting in sub-standard vaccines. Vaccines are a global production and they can be automatically approved in many countries based on clinical trials that were performed in another country. Manufacturers in the US have less incentive to develop safe and effective vaccines because they are exempt from liability when harm is caused. This legislation ensures that there is a stable vaccine market but it does not provide incentives to protect the health of the population. Government regulators in most countries are 100% funded by industry under a Cost-Recovery (User-Pay) system. This means they approve their sponsor's vaccines/drugs for the market and monitor these same products for safety and efficacy. In effect they are indirectly monitoring their own products. Large political donations from pharmaceutical companies are also being allowed to influence government policy. Funded lobby groups are targeting policy decision-makers, medical practitioners, educational boards and mainstream media with selective information. Vaccine advisory boards are rife with conflicts of

interest, enabling industry to influence the direction of government funding in health policy research and policy decision-making. National vaccine advisory committees such as ATAGI have been established in many WHO member countries and they receive advice and financial support from the WHO in the development of national vaccination programs. Recommendations for new vaccines are not always founded on local data and cost-effectiveness is being determined using economic models that rely on non-transparent assumptions about the safety and efficacy of vaccines. Although the importance of vaccine-created herd immunity is used to promote vaccines to the community, the chairman of ATAGI for the last decade states that the implications for herd immunity for new vaccines are 'neither necessary nor sufficient for a positive recommendation for NIP suitability' (Nolan 2010 A79). This indicates that vaccines are being promoted to the community on a false premise that has serious implications for population health. Further, the cost-effectiveness of vaccines is being determined on evidence produced in clinical trials that are funded by pharmaceutical companies and carried out by researchers/chief investigators who are representatives on government vaccine advisory boards such as ATAGI and the NCIRS.

This arrangement is very profitable for universities, governments, researchers and representatives on vaccine advisory boards but it is extremely costly to public taxpayers and to population health. In 2008-2009 the cost of providing vaccines 'free' to Australians was well above $AU400 million (Nolan 2010 A76). However, the actual cost of these programs is unknown because the figures are not released to the public (even when requested) and they do not include the cost to the community of the deaths and disability that are a known side-effect of vaccines. This cost to the community is unknown because the TGA has not established an active surveillance system that can make causal relationships to vaccines. A regulator that is 100% funded by industry has no incentive to accurately monitor the adverse events from its own products. This demonstrates the need for vaccination policies to be independent from commercial and political interference in order to protect public health. In Australia policy decisions for vaccination programs are based on research (often unpublished) that is performed by government representatives on vaccine advisory boards who receive honoraria and funding for their clinical trials from pharmaceutical companies. The findings from such research are being used in policy

decisions for vaccination programs without public scrutiny or assessment by independent researchers.

In chapter 7 I discuss the evidence the Australian government is providing to the public to support the claims about vaccine safety and efficacy. Chapter 8 presents a description of undone science and the political framework that leads to a lack of integrity and rigour in medical science. Chapters 9 and 10 are case studies of the HPV vaccine and 'Swine Flu' 2009 vaccine, showing the influence of corporations in the development of global vaccination policies. Chapter 11 presents the conclusions for this investigation.