Pharmaceutical Sponsorship and Relationship with Industry

Background

What are industry and sponsorship
The Australian Medical Students’ Association (AMSA) is the peak representative body for Australia’s 17,000 medical students and future prescribers. As such, at all times AMSA should make consideration for the best outcomes for patients, in line with the professional values of the Good Medical Practice code of conduct for doctors in Australia (1). Decisions about treatment and prescribing have a significant impact upon patient outcomes; therefore, influence by medical industry upon patient management is an issue of importance for Australia’s medical students. Medical industry in Australia includes the pharmaceutical industry, medical device and technology industry, and other health care product suppliers, health care facilities and medical services (2). Medical devices and technology includes any devices used for the diagnosis or management of patients. Pharmaceuticals include all products listed as ‘medicines’ under the Therapeutic Goods Administration (TGA) Australian Register of Therapeutic Goods (3). Relationship between AMSA, Australian medical schools, and medical students includes all interactions with medical industry, with specific emphasis on marketing, donations, sponsorship, educational events, remunerations and gifts (1).

Conflicts of interest
As defined by the Medical Board of Australia, “conflict of interest in medical practice arises when a doctor, entrusted with acting in the interests of a patient, also has financial, professional or personal interests, or relationships with third parties, which may affect their care of the patient”(1). Placements in hospitals and clinics are a fundamental core of medical education. Consequently, medical students are also exposed to these relationships and influences.

These relationships may offer financial, material or career-orientated contributions to both healthcare professionals and students. These extend, but are not limited to: (2)
- Receiving gifts: clinic visits, meals, sample medical packs etc.
- Royalties (e.g. research contribution, drug and device development).
- Financial compensation and speaking opportunities at educational events.
- Fellowships.
- Employment opportunities.

It is acknowledged that multiple interests are common in practice and are generally appropriate. Nevertheless, future doctors should recognise the propensity for conflicts of interests (COI) especially in a profession commonly the focus of vested interests. In line with patient-centred practice, when faced with COIs, a medical professional has their primary duty towards their patient and must act accordingly to their best interests. It is important that students recognise these COIs and are able to resolve them appropriately.

Regulation of pharmaceutical and medical device marketing
In Australia, marketing by the pharmaceutical industry is heavily restricted. Direct advertising of pharmaceuticals to consumers is prohibited by the Therapeutic Goods Act 1989, although the Act does not prohibit advertising of medical devices (4). Advertising to healthcare professionals is permitted; however, per the Competition and Consumer Act 2010, it must only involve promotion of indications for which the medicine is registered (5). It is a condition of registration of a medicine with the TGA that its marketing also adhere to the Medicines Australia code of conduct (6).
This code of conduct restricts the ways by which pharmaceutical companies can advertise medicines. For example, the code expressly prohibits the provision of gifts such as stationary to health care professionals. Funding to speak at conferences, commensurate with the work done, and meals may be provided to health care professionals under the code (6).

Pharmaceutical companies may also sponsor educational events, including those that involve medical students. In all instances, the purpose of this funding must be to enhance medical knowledge and improve the quality use of medicines. Sample medications may be provided by pharmaceutical companies, for reasons including “gaining familiarisation with the product” and “the use of alternative treatments prior to writing a prescription”. Providing gifts or money to health care professionals with the stated expectation that they will prescribe a drug is not permitted under states’ bribery laws (7).

Under the Medicines Australia Code of Conduct, pharmaceutical companies must disclose any transfers of value made to health care professionals, except for meals. This includes, but is not limited to, hospitality to attend conferences and speakers’ fees. To make the disclosure, the pharmaceutical company must obtain consent from the health care professional. Disclosure without consent is likely to breach the Privacy Act 1988 (7, 8). There is no requirement for medical devices manufacturers to disclose transfers of value to healthcare professionals.

The Australian Medical Council, which is responsible for accreditation of medical schools, makes specific mention of conflicts of interest in its standards for accreditation (9). The Standards require that medical schools equip students with the ability to critically appraise literature and contribute to evidence-based medicine, as well as understand the impact of financial conflicts of interest. The Australian Medical Association, in its policy on the relationship between doctors and industry, calls on medical schools to provide “formal training referring to ethical relationships with industry” (10).

Although some countries have found different ways to regulate the pharmaceutical industry, Australia’s regulatory framework is not an outlier. The United States and New Zealand are the only countries that allow direct advertising of pharmaceuticals to consumers (11, 12). Transfers-of-value to doctors must be reported in the USA under the Physician Payments Sunshine Act 2010 and in the EU under the EFPIA Code (11, 13). The penalties for failure to disclose are particularly strong in the US.

Australia’s regulatory framework regarding educational events is in line with those of the US, EU and UK (14). The provision of medication samples is much more strongly regulated in the UK and certain EU countries. In the UK, samples of a certain product may only be provided four times in one year and only if the doctor has submitted a written request to the company (15). Dutch legislation is more stringent, requiring that samples of a product only be provided once every two years (16).

Potential negative implications of the interaction between health professionals and industry

Studies indicate that interactions with pharmaceutical companies - including visits from sales representatives, advertisements in journals, sponsored educational sessions, information received via mail, prescribing software and sponsored clinical trials - may be associated with negative prescribing behaviours among doctors to the potential detriment of patient outcomes and health care resources (22-28). A systematic review in 2010 found that where a significant association was discernible, it took the form of increased rates of prescribing, prescribing that was less aligned to prescribing guidelines or increased prescribing of more expensive branded drugs even when such prescribing was not supported by scientific evidence (22). Of added concern is that in spite of this evidence, studies suggest that many doctors consider themselves immune from potential influence, even though many consider large proportions of their colleagues would not be (22, 23, 25, 29).

There is evidence that similar attitudes are held by medical students. A systematic review indicates that medical students exposed to direct-to-clinician advertising during their studies may develop a more positive attitude towards the practice, although many students believe themselves immune to bias (24). A similar blind spot among students to their vulnerability to potential bias has been echoed in more recent overseas studies (25, 29, 30). Students who received small promotional items have also been shown to develop implicitly positive attitudes towards the relevant brands (31). However, the same study found more skeptical attitudes towards pharmaceutical companies among senior students who had attended a medical
school with more restrictive policies regarding interactions with pharmaceutical companies. Among medical students, higher levels of exposure to pharmaceutical branding has also been correlated with inferior knowledge of evidence based prescribing principles and an increased likelihood to select brand name pharmaceuticals (32). On the other hand, there is evidence that restrictions on student and/or resident interactions with the pharmaceutical industry and education about ethical issues is associated with industry interaction that results in more critical attitudes towards industry and less overall contact (23, 25, 33) and in one study of psychiatric residents in the US, higher quality prescribing (34).

There remains a need for further research to better illuminate the causal relationship (in contrast to association) between interactions with the pharmaceutical industry and the behaviours and attitudes of doctors and medical students. However, the wide body of evidence regarding the interactions between the pharmaceutical industry and doctors and students and the attitudes underpinning them have seen efforts by various stakeholders in Australia and overseas to address the potential for conflict of interest (25). These concerns have been particularly prominent in the US, which saw Senate investigations and recommendations from professional medical associations to increase education and implement policies to guard against improper industry influences, in addition to initiatives from the American Medical Students’ Association such as the PharmFree Scorecard which rates medical schools on their conflict of interest policies (25). Other initiatives by doctors and students to highlight these ethical issues included the NoFreeLunch campaign, PharmedOut (25) and in Australia, the doctors’ organisation No Advertising Please (35) and the student organisation Pharma Phacts (36). In Australia, concerns have been raised regarding the need for more cohesive efforts to educate students about potential conflicts of interest with industry and implement policies to address this, particularly compared with the more rigorous examples from some US medical schools (26, 28, 35, 36).

Additionally, there are concerns regarding the accuracy and potential bias of information and studies funded by pharmaceutical companies (25). The misrepresentation by pharmaceutical company Purdue of the addiction risk of the opioid OxyContin and the opioid abuse crisis in the US following extensive marketing highlight the risks associated with competing educational and commercial interests (37), as do other instances of pharmaceutical companies being fined for providing misleading information or withholding information about their products (38). A 2017 cross sectional study showed that randomised trials run by investigators with financial ties to drug manufacturers were more likely to show positive results than trials conducted by independent researchers (39). A Cochrane Review in 2017 found that the results of studies funded by pharmaceutical or medical device companies suggest an industry bias in favour of the sponsors’ product that cannot be accounted for by risk of bias assessment (40). So-called ‘marketing’ or ‘seeding’ trials may also be funded by industry with the intention of increasing awareness of existing products. Critics allege that these trials ‘subvert the scientific process and violate ethical norms’ by disguising marketing behaviour as legitimate research (41).

**Publication bias**

Withholding information is becoming a more worrying issue given industry or commercial bodies are responsible for around 300-400 trials annually in Australia (42). Publication bias refers to trials with positive outcomes being published more frequently than others. Unsuccessful trials are stopped early or simply not published (43). The result of which can create a distortion that leads to the overstatements of treatments. In 2005, the International Committee of Journal Editors recommended compulsory registration of all trials, however even in 2014, half of all editors worldwide considered registration of randomised clinical trials as a factor in publishing (44).

Along with biased estimates of treatment effects, publication bias can cause overlapping research and wastage of resources for other medical researches (45). Unfortunately, the effects of this bias extend to a substantial number of study participants being exposed to the risks of trial participation without the benefits that accompany the publication of complete trial results (46, 47). Another way in which pharmaceutical companies have been shown to use publication bias is by commonly publishing at symposiums where peer review is less frequent and results often support the sponsor (48). In fact further research by Rochon and colleagues showed the efficacy described in these particular studies were often unsubstantiated (49).

As a response to publication bias, the **Australian and New Zealand Clinical Trials Registry (ANZCTR)** was created. In 2007, it was recognised by WHO as a primary registry of clinical trials where researchers register their trials, voluntarily and for free (42, 50). This means trials that are not completed or published will still be recorded and this appears to be the opinion of
the international community (51). At the moment, any trials that are registered must include information about the funding of the project, treatments being tested, objectives and the sample size and recruitment status but not the specific outcomes of the trial (50, 52).

Benefits of the relationship between industry and healthcare professionals

Medicines Australia sets out guidelines for promotion of medicines by pharmaceutical companies and stipulates that ethical, open and transparent interactions with the industry are necessary for safe, effective and quality medicines (1). It is important to note that Medicines Australia allows industry relationships with healthcare professionals as long as these relationships are for improving knowledge about medicines and their quality use. Similarly, the mission statements of pharmaceutical companies such as Bayer and Astra Zeneca primarily focus on innovation and solutions for the betterment of human health. In fact, pharmaceutical companies are especially needed for research and development (R&D) of novel medicines which is an expensive process. It costs over one billion US dollars to develop a new drug and governments cannot possibly fund such high-risk products (17). Despite some of the criticisms the industry has attracted, pharmaceutical products are ubiquitous and without them there would be no medicines to prescribe. Additionally, not all pharmaceuticals are fraught with controversies, a study in 2004 calculated that close to 27 new chemical entities and several biologics a year were developed in 1990s and it has been shown that these developments have contributed to prolonging life and reducing hospital stay (18). Examples of recent pharmaceutical successes include the development of Gardasil® vaccine in Australia, (19) statins (20) and promising cancer treatments tailored to genetic mutations such as BRCA1/2 (21).

Medicines Australia is the national representative lobby for the pharmaceutical and medical device industry, representing more than forty Australian and international companies. (1) This body sets out guidelines for promotion of commercial products, and stipulates that ethical, open and transparent interactions with the industry are necessary for safe, effective and quality medicines. Medicines Australia advocates that companies should form relationships to improve clinicians’ understanding and use of their products, with any ensuing financial sponsorship, speaking fees or event support disclosed on a public register. Proponents of industry relationships with clinicians cite the high cost of developing modern pharmaceuticals, (17) and the commercial necessity to return a profit to investors during the relatively short period of patent protection, as justifying promotion to clinicians. While some novel drugs have attracted controversy because of their high price or perceived lack of efficacy, a review of drugs approved during the 1990s showed that the use of new agents “contributed appreciably to the extension of life spans and the reduction of hospital stays.” (18).

Position Statement

1. AMSA believes that as future prescribers, medical students have a responsibility to ensure prescribing for the best patient outcomes in line with available evidence;
2. In light of the evidence of influence upon prescribing, AMSA does not undertake sponsorship or partnerships with pharmaceutical companies; and
3. AMSA supports the right of individual students to excuse themselves from sessions involving pharmaceutical advertising in their education or extra-curricular activities.

Policy

AMSA calls upon:

1. The AMSA Executive and its subcommittees, including but not limited to events and sponsorship teams, to:
   a. Be open and transparent with members and medical students about all sponsorship received;
   b. Not accept sponsorship, or enter into partnership arrangements with, pharmaceutical companies
   c. Cautiously consider sponsorship, or entering into partnership arrangements with medical device companies, where there is a reasonable basis to believe that there could be an association between the sponsorship or agreement and the medical devices produced by that company;
      i. In the first instance, the Executive should interpret the background to this policy in determining if a company falls into this classification, with
regard to the products produced, their listing with relevant bodies and use in Australian prescribing.

ii. Where it is unclear if a company falls under the definition of pharmaceutical or medical device company, the Executive should refer the matter to the members for consideration.

d. Continue informing themselves about measures taken by other medical schools, student organisations or other professional bodies, both domestically and internationally, which may be relevant for Australian medical students. These would include:
   i. Measures in raising awareness about conflicts of interests arising from interactions with pharmaceutical industries and medical device companies.
   ii. Policy and measures addressing and preventing potential conflicts of interests.
   iii. Evidence of this awareness through AMSA publications and/or the introduction of initiatives to enhance awareness of industry influence for its members.

2. Medical student societies:
   a. Take all reasonable steps to cease any pre-existing sponsorship or partnership arrangements with pharmaceutical companies in a timely manner;
   b. Closely reconsider pre-existing sponsorship or partnership arrangements with medical device companies in a timely manner;
   c. Not accept sponsorship, or entering into partnership arrangements with, pharmaceutical companies
   d. Cautiously consider sponsorship or partnership arrangements with medical device companies, where there is a reasonable basis to believe that there could be an association between the sponsorship or agreement and the pharmaceuticals or medical devices produced by that company;
   e. Make it an ongoing priority to inform itself about any measures to raise awareness of and address the issue of potential conflicts of interest arising from medical students and medical professionals interacting with the pharmaceutical and medical devices companies and consider whether they may be applicable for medical students in Australia;
   f. Advocate to their respective medical schools regarding the importance of educating medical students about the evidence of the potential negative effects of interactions and the risks of conflict of interest associated with pharmaceutical and medical device companies;
   g. Take all reasonable steps to raise awareness among medical students regarding the evidence of the potential conflicts of interest which can arise from interactions with pharmaceutical and medical device companies and advice for managing such conflicts and raising awareness about options for locating independent medical information.

3. Australian medical schools to:
   a. Ensure that medical students receive comprehensive education regarding conflicts of interest, consistent with requirements in the AMC standards, including:
      i. Quality, up-to-date, unbiased and evidence-based teaching on medical devices, pharmaceuticals and prescribing;
      ii. Evidence-based teaching on the legal framework surrounding pharmaceutical and medical device marketing and its impact on prescribing;
      iii. Skill teaching regarding critical appraisal and sourcing of independent evidence;
      iv. An overview of drug development and approval;
   b. Ban formal education given by pharmaceutical and medical device companies at medical schools;
   c. Ensure students are not penalised for non-attendance at any educational or other university organised sessions provided by industry;
   d. Refuse to accept sponsorship or donations from industry that is not for the purpose of research;
   e. Declare all funding from industry annually.

4. Australian medical students to, over the course of their training:
a. Develop a nuanced understanding of the role of industry in modern medical practice;
b. Carefully consider decisions about event attendance, scholarship acceptance and involvement in industry-sponsored research;
c. Exercise their right to non-attendance of industry-sponsored events, if desired.

5. The Australian Government to:
   a. Make ANZCTR registration mandatory for all clinical trials before the commencement of the trial and that all research that makes reference to a future treatment, is to be registered with ANZCTR;
   b. Mandate that all trials registered with ANZCTR to include an outcome of research;
   c. Further restrict the distribution of medication samples to doctors;
   d. Fine companies or researchers who fail to submit for publication results of a clinical trial that enrolls patients in Australia in a timely manner, in the absence of exceptional circumstances;
   e. Restrict pharmaceutical and device company education in hospitals to instructional rather than promotional content.
   f. Mandate full disclosure of expenditure at educational events by pharmaceutical and medical device companies, including cost of transporting speakers, speaker fees, food, beverages, residential costs and other associated expenditure;
   g. Consider the role of legislation to address the issues of potential conflict of interest, associated with the relationships between the pharmaceutical industry and health professionals, and with the wider community;
   h. Mandate that pharmaceutical and medical device companies fully disclose, in a timely manner, any meals, gifts or other incentives offered to hospitals, medical practices or individual clinicians by pharmaceutical companies;
   i. Mandate that hospitals, medical practices or individual clinicians disclose to patients and staff any sponsorship for meals, gifts or other incentives offered by pharmaceutical and medical device companies;
   j. Continue to ban direct-to-consumer advertising of prescription medication;

6. Representative groups for medical professionals, including the Australian Medical Association (AMA), to:
   a. Ensure all relationships with industry are ethical, compatible with best practice and not biased by conflict of interest;
   b. Not accept and encourage their members not to accept gifts, sponsorship, compensation for services and research funding from industry;
   c. Make publicly available records of all donations, sponsorships, remunerations and gifts from industry to the representative groups including;
   d. Minimise prescription bias to the best of their ability in line with recent evidence;
   e. Encourage their members to seek education on pharmaceuticals and medical technologies from unbiased, peer reviewed publications rather than company representatives;
   f. Promote a structured education program for relationship with industry, in line with AMC guidelines, to be implemented in medical schools.

7. AMSA members reserve their right to request further information about the nature of any and all sponsorship or partnership agreements. The members may from time to time set additional standards to support the language of this document insofar as doing so contributes to the company's public policy objectives.

References
1. Australia M. Code of Conduct 18 ed 2015
5. Competition and Consumer Act 2010 (Cth) (Austl.).
14. EFPIA code on the promotion of prescription-only medicines to, and interactions with, healthcare professionals. Brussels: European Federation of Pharmaceutical Industries and Associations; 2014.
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Policy Details

Name: Pharmaceutical Sponsorship and Relationship with Industry (2018)

Category: H - Ethics

History:
Adopted Council 3, 2014
Reviewed Council 2, 2018 - adopted