Conflicts of Interest in Biomedical Research

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Abstract: Focusing on financial conflicts of interest policies in Singapore and in the US, this paper argues there is insufficient recognition of science as a profession. Coupled with growing commercialisation, this deficiency could undermine the long-term viability of biomedical sciences.

Conflict of interest (COI) is a well-recognised concern in a fiduciary relationship, where the agent is expected to act in his or her principal’s best interests. Some of these relationships of trust include those between doctors and patients, lawyers and clients, and bankers and customers. A conflict arises when either the agent’s private interest or an obligation owed to another party prevents the agent from acting in the principal’s best interests. A conflicting interest need not result in actual interference with the principal’s best interests, since potential interference is sufficient to create a conflicting interest on the part of the agent. Hence in a commercial setting, self-dealing or misappropriation of confidential information for personal gain is a conflict of interest even when the principal suffers no direct harm (Supreme Court of Singapore 2000).
In biomedical research, a similar element of exploitation of an agency or trust relationship underlies various definitions of COI. Rodwin (1993) considers conflicts broadly as involving competing loyalties, whereas others understand COI to arise when a researcher’s judgment concerning a primary interest (such as a patient’s welfare or some other professional, ethical or legal obligation) is unduly influenced or compromised (Thompson 1993; US National Human Research Protections Advisory Committee 2001: Section 2; Shamoo and Renik 2009: 191). COI can be apparent or actual, and can relate to an individual or an institution. In Singapore, the Bioethics Advisory Committee (BAC) defines COI (in relation to institutional review boards or IRBs) as circumstances that adversely affect impartiality, objectivity and independence, and encapsulates both actual and potential conflicts (BAC 2004: paragraph 4.17 and 5.58).

On institutional COI, the BAC identifies the independence and ethical integrity of IRBs in the exercise of their powers and duties as fundamental underlying principles. These principles require both IRBs and their institutional hosts to be aware of any potential or apparent COI, and to take reasonable steps to avoid and minimise conflicts. A recommendation put forward by the BAC is for an IRB to prepare a special report on all reviews of research programmes in which there is an actual, potential or apparent COI, for submission directly to the board of directors of its host institution (BAC 2004: paragraphs 5.36 to 5.41). On the part of researchers, the BAC indicates that it is important for researchers to take special care to avoid any form of COI, whether actual, potential, or merely an appearance of conflict as such. To ensure objectivity in the review process, researchers should not be involved in, or give the appearance of being involved in, the ethics review and approval process of any project that they are involved in (BAC 2004: paragraphs 6.14 to 6.15). Similarly, if a member of an IRB has a personal interest in the research under review, that member is required to recuse himself or herself from any consideration of the case, and refrain from offering his or her opinion. In addition, similar conflicts could arise where a researcher is also the administrative custodian of patients’ medical information, or attending physician. In relation to the latter, and drawing reference to Article 23 of the Declaration of Helsinki, the BAC requires a researcher physician to be aware of a potential COI and of the fact that their patients may feel obliged to give consent (BAC 2004: paragraphs 5.62, 6.36 and 7.14).

Transparency through disclosure as a means of addressing conflicts situations has been emphasised by the BAC. It states that researchers have a duty to make a declaration of any conflict, to give full disclosure of the facts giving rise to such conflict, and to detail the steps proposed or taken to minimise or avoid the appearance of actual or potential COI. An IRB member who is similarly conflicted is also required to make full disclosure (BAC 2004: paragraphs 5.63 and 6.14). One such conflict noted by the BAC is financial COI. The BAC states that potential research subjects may need to be informed of any financial arrangements offered by corporate sponsors to researchers or their institutions (or both). This disclosure is understood as facilitating understanding and advance the ethical goal of informed consent (BAC 2004: paragraph 5.40).

Tragic incidents, like the death of gene therapy patient Lea Kushner in 1999, make clear the importance of disclosing financial COI (Gelsinger 2006). Since that time, policy-makers in the US have given clearer guidance on when and how such conflicts are to be disclosed. Under the ‘Final Rule’ of the US Department of Health and Human Services (DHHS), all “significant financial interests that could directly and significantly affect the design, conduct or reporting of research” must be disclosed to institutional officials (DHHS 2011: §§ 50.604 and § 50.605). Financial interests are significant when a remuneration or equity interest (in a public company) of US$5,000 or more is entailed. The ‘Final Rule’ further sets out certain exclusions and inclusions, as well as procedural and informational requirements. In addition, the DHHS has issued a separate set of guidance on financial relationships and interests (DHHS 2004), and other agencies (such as the US Food and Drug Administration) have similar policies on COI. These policies make clear that neither researchers nor their sponsoring institutions are prohibited from having financial interests in their research. Other than drawing attention to the risk of compromises, the underlying actual and potential conflicts remain. Other persistent concerns have been noted as relating to a number of issues including quality of clinical trials, independence of the investigators and of the research organisation, premature trial termination for financial reasons, censorship or delay in publishing, and low publication rates of negative trials or poorer quality of publications resulting from industry-sponsored research (Ferris and Naylor 2006: 109–110).

With growing emphasis on industrial collaboration and commercialisation of research, concerns over financial COI are likely to exacerbate. In recent years, the use of contract research organisations (CROs) have been controversial as there is a very direct financial COI, given that CROs are conceivably under pressure to deliver positive trial results in order to sustain business relations with their pharmaceutical clients. In countries like the US and Canada, these concerns are worsened as ethics review have often been undertaken by for-profit IRBs. While there is currently no clear evidence that COI is correlated with scientific fraud or other serious ethical violations, funding sources do have some influence over research outcomes (Krimsky 2006: 72–77). Even if methodological rigour is not compromised, the general perception of science as ‘objective’ could be undermined. In the long run, growing commercialisation of science could compromise scientific quality, research participant welfare and public confidence, unless more active measures are introduced.

John Boatright explains that prohibitions against COI in medicine and law are founded on the structure of a profession; or self-perception by a doctor or a lawyer. In contrast, the standards that a financial service provider must adhere to are largely determined by the terms of the financial contract rather than a professional role (Boatright: 132–133). By focusing only on disclosure, current policies on COI appear to present science more as a service rather than a profession.
than a profession. More critically, such an approach fails to recognise scientific enterprise and scientific integrity as societal goals. Currently, financial arrangements of institutions with industry sponsors are not actively regulated. A difficulty with this approach is that, by relying on individual research institutions to provide assurance that COI is managed, it cannot ensure a level playing field. Some institutions may be concerned that they risk losing investigators to other institutions with more lenient policies (Perlman 2010). With inadequate checks and balances to guide institutions, together with severe budgetary and fiscal pressures, not to mention the competition for talent and reputation at institutions of higher education, COI may well be a very real threat to the long-term credibility and viability of science.

To be sure, the production of new knowledge and drugs promotes social welfare in improving clinical conditions and the quality of life, as well as reducing mortality and morbidity rates. However, intermeshing scientific interests with corporate ones could significantly undermine public trust in clinical research. It is argued that ethical and legal norms must be recognised as critical in securing not only the social objectiveness (especially in terms of public confidence), but also the cognitive rigour, of science.

References


Supreme Court of Singapore: Chew Kong Huat and Others v Ricwil (Singapore) Pte Ltd [2000] 1 SLR 385


About the Author

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