

# Conflict of Interest in Clinical Research: Direct Payment to the Investigators for Finding Human Subjects and Health Information

*P. Saradhi Puttagunta, Timothy A. Caulfield  
& Glenn Griener*

## **Abstract**

The recent death of teenager Jesse Gelsinger in a drug therapy trial has drawn attention to how financial conflicts of interest may compromise patient protection. While research institutions throughout the world have instituted a variety of conflict of interest guidelines, the potential conflicts associated with investigators receiving direct payment from private companies for both the recruitment of patients and the running of clinical trials in pharmaceutical research remains a relatively unexplored area. Clinical researchers undoubtedly deserve to be reasonably compensated for their participation. But these incentive mechanisms also have the potential to create conflicts of interest – both real and perceived.

### These conflicts include:

- ▶ Erosion of informed consent;
- ▶ compromise of patient confidentiality;
- ▶ enrolment of ineligible subjects.

The purpose of this paper is to examine the issue of physician remuneration for patient recruitment and conducting clinical trials for pharmaceutical companies. The potential conflicts and dangers of this remuneration scheme will be examined in detail, as will be the lack of guidelines. This lack of guidelines poses a problem for research ethics boards in trying to protect patients' rights.

## **Conclusion**

The authors conclude with recommendations as to which legal mechanisms can best be implemented to effectively alleviate this conflict of interest. Specifically, the authors consider:

1. full disclosure to the patient of the doctors' financial interest;
2. national/international guidelines to maintain consistency of rules and to prevent 'forum shopping' by drug companies;
3. education of clinical investigators on the issue of conflicts of interest; and
4. implementation of regulations specifying exactly how much doctors are to be paid for clinical trials.

## The Issue

More and more doctors in private practice are being recruited to run industry-sponsored trials. This trend arose in the last twenty years when government funding for

subjects' safety. No specific legal framework exists in Canada to govern REB practice. However, guidelines and policies do exist. These include:

- ▶ Private corporations have been the largest sponsors of pharmaceutical research in both Canada and the United States in the last twenty years.
- ▶ The number of private doctors performing research is on the rise. In 1990, 4 307 private practice doctors carried out research in America. By 1997, that number increased to 11 662.  
K. Eichenwald & G. Kolata, "Drug Trials Hide Conflicts for Doctors" *New York Times* (16 May 1999)

clinical drug trials declined, and industry funding increased. For pharmaceutical companies, this accelerates the time it takes to test, approve, and put a new drug product on the market.

## Concern

While doctors have a right to be reasonably remunerated for the work they perform, inappropriate remuneration raises the possibilities of:

- erosion of the patient's informed consent;
- compromise of patient confidentiality (by doctors searching other doctors' patient databases for prospective test subjects);
- enrolment of ineligible subjects or subjects on the margins of eligibility;
- marketplace pressures leading to declines in patient safety;
- a coercive enrolment environment, e.g., patients agreeing to be subjects simply because they fear losing the caregiver if they say 'no'; and
- doctors, under pressure to increase their income, being inclined to perform research that they are not qualified to do.

Past experience shows that a financial interest can bias a physician's decision-making.<sup>1</sup>

## The Current Regime

The main players in a drug trial are Health Canada, the investigator, the patient, the sponsor, and the Research Ethics Board (REB). In Canada, REBs help protect human

- 1) **TriCouncil Policy Statement (TCPS).** This document governs all research that receives federal funding. Researchers, it states, have a fiduciary relationship with their subjects. The TCPS advocates a "proportionate" approach to conflicts: if the conflict of interest is small, the investigator need only disclose the interest. If the conflict is large, the investigator must abandon one of the interests or withdraw from the trial.<sup>2</sup>

As a general guide, per capita payments should be comparable to the physician's or researcher's usual professional fee.<sup>3</sup>

- 2)
- 3) **Good Clinical Practice Guidelines (GCP).** These are internationally developed standards. Researchers who obtain private funding often follow them.<sup>4</sup>
- 4) **Canadian Medical Association Guidelines.** These apply to the relationship between doctors and industry. They state that a doctor's primary obligation is to the patient. Any relationship with industry must not affect this obligation.<sup>5</sup>
- 5) **Others.** These include the Helsinki Declaration, the International Guidelines for Biomedical Research Involving Human Subjects, and the Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products from the World Health Organization.<sup>6</sup>

## Problems with the Canadian System

Many problems have been identified with Canada's REB system. Some problems relevant to this issue include the following:

- Guidelines are helpful, but they are often ambiguous and not always enforceable.
- The Canadian system needs regulations that can be enforced by REBs. REBs may have trouble addressing the remuneration issue without specific guidelines, for example.
- There is variation in practice between REBs.
- REB members are vulnerable to institutional pressure.

## **What Is Needed to Rectify this Problem**

1. Ensure patients know of the conflict of interest.
2. Mandate the disclosure of relevant contracts and detailed research budgets.
3. Ban certain situations that lead to a conflict of interest. For example:
  - attempt to define and consider banning excessive remuneration.
4. Define what constitutes allowable reimbursement for investigators. These can be:
  - time spent managing patients and the project;
  - salaries of coordinators and fellows; and
  - overheads and miscellaneous expenses.<sup>7</sup>
5. Mandate training programs for investigators and REB members. This will help to ensure that all relevant parties understand conflict issues.
6. Implement a system to accredit and monitor REBs, especially independent ones.
7. REB panels need to include others. To broaden the perspectives of REB panels, members from outside the research community should be included. For example, members of groups representing human subjects may serve on REBs.
8. Implement consistent conflict of interest guidelines/regulations nationally. This is to prevent forum-shopping by industry. These rules should apply to both researchers and institutions.

---

*P. Saradhi Puttagunta is a third-year law student, at University of Alberta and a Research Assistant at the Health Law Institute. Timothy A. Caulfield is a Canada Research Chair in Health Law and Policy, Associate Professor, Faculty of Law and Faculty of Medicine & Dentistry, and Research Director, Health Law Institute, University of Alberta. Glenn Griener is a Professor in the Department of Philosophy, University of Alberta. This article*

*was presented as a poster at the Canadian Bioethics Conference held in Winnipeg in October 2001. Special thanks to Tania Bubela, Sarah Schwann and Nina Hawkins.*

1. H. Stelfox *et al.*, "Conflict of Interest in the Debate over Calcium Channel Antagonists" (1998) 338 *New Engl. J. Med* 101; R. Davidson, "Source of Funding and Outcome of Clinical Trials" (1986) 1 *J. Gen. Int. Med.* 155; ? M. Cho & L. Bero, "The Quality of Drug Studies Published in Symposium Meetings" (1996) 124 *Annals of Int. Med.* 485; and M. Friedberg *et al.*, "Evaluation of Conflict of Interest in Economic Analyses of New Drugs Used in Oncology" (1999) 282:15 *JAMA* 1453.
2. *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (Ottawa: Supply and Services Canada, 1998), art. 4.1-4.2.
3. *Ibid.*, art. 7.4.]
4. Good Clinical Practice: Consolidated Guidelines, International Conference on Harmonization of Technical Requirements for Regulation of Pharmaceuticals for Human Use, 4 April 1996, Draft 9 Step 2. ICH Expert Working Group. Online: <<http://www.ncehr-cnerh.org/english.gcp/>>
5. Canadian Medical Association. "CMA Policy: Physicians and the Pharmaceutical Industry" (2001) 164:9 *Can Med J.* 1339.
6. World Medical Association Declaration of Helsinki, adopted by the 18<sup>th</sup> World Medical Assembly, Helsinki, Finland, June 1964. International Ethical Guidelines for Biomedical Research Involving Human Subjects, Council for International Organizations of Medical Sciences (CIOMS) 1993, adopted by the World Health Organization.
7. A. Rutherford & W. Johnston, "Potential Problems with Industry-Supported Research", (May 2000) 31 *J. Vas. Surgery* 1066.