EDITOR'S NOTE: *In the past several months, there have been a number of publications, in both the academic literature and the popular press (such as* The Wall Street Journal *and* The New York Times*), that have been critical of clinical investigators who have entrepreneurial relationships with pharmaceutical houses, instrument manufacturers, and other businesses active in the medical, dental, and scientific fields. In reviewing the literature, the Editor has not found responses to these criticisms from either the business world or the clinical investigators in question. The lack of response is understandable if there is an overall perception that such scientists are in some way tainted or dishonest. There is little doubt that they have been placed in a defensive position. However, few issues are so clear cut that alternative viewpoints do not exist. The Editor has therefore asked Mr. Lewis Pell to present his views. Mr. Pell has founded and is Director of many medical device companies, including Versaflex Delivery Systems, Vascu-Care, Pentax Precision Instruments, American Endoscopy, and most recently Heart Technology Inc., which has developed an atherectomy device for the removal of coronary and peripheral arterial plaque. The device is currently undergoing clinical trials to meet Food and Drug Administration (FDA) requirements. Mr. Pell is closely aligned with the readership of this journal as the Chairman of Vascu-Care, which is the owner of Machida America, and through his role with Pentax Precision Instruments. Both companies manufacture flexible fiberoptic nasopharyngoscopes used by much of our readership. He is also President of OPAC Corporation, which is a medical venture capital company based in Seattle.*

Editorial

LEWIS PELL

I have been following with interest a recent series of publications regarding the issue of the ethics of physicians and other clinical scientists who have financial interests in their own research. Articles and editorials on this issue have appeared in *The Wall Street Journal, The New York Times, JAMA,* and *The New England Journal of Medicine,* and there is little doubt that the authors take a dim view of investigators who benefit financially from their research. Arnold S. Relman, M.D., has published several papers on this topic (Relman, 1980, 1984, 1985, 1988), as have other authors (Dobson et al, 1986; Hyman and Williamson, 1989). Most recently, Relman (1989) wrote an interesting and articulate editorial on financial conflicts in clinical investigations. Relman concludes that a clinical investigator who has a financial stake in a company represents a conflict of interest and is inherently unethical. Is this to be accepted as fact without challenge? Is this type of potential financial benefit by investigators a unique and condemnable practice? In fact, Relman does not address the more subtle, but more frequent conflicts that permeate the medical profession on a daily basis without the checks and balances that are inherent in all clinical investigations.

A physician who has a financial interest in a company with which he or she is a clinical investigator can certainly realize positive financial benefits from the outcome of the investigation's results. However, this is consistent in many phases of medical studies and/or practice. The outcome of research can have an effect on the awarding of grants, on opportunities for promotion, and, of course, on professional reputation. There is no doubt that the research (including clinical trials) of health professionals may have an effect on the personal financial interest of the investigator, regardless of his or her involvement with the business world. For example, a surgeon in clinical practice would certainly have a financial incentive if a particular operation he or she has described in the literature proved to be beneficial in clinical trials. Referrals for the operation would increase, and the surgeon's income would increase concomitantly; this is hardly a hypothetical situation. Is it less of an ethical quandary than other forms of entrepreneurship?

Regulations have been imposed recently in an attempt to curb conflicts of interest, but even so, the primary safeguard remains the ethics and professionalism of the investigators. Although there has been occasional malfeasance, by-and-large the public has been well served by honest, dedicated, and ethical professionals. In this respect, there is little difference between scientific investigation and clinical practice.

With regard to clinical trials, mechanisms already exist to protect the public. First, the conduct and analysis of all clinical trials remain the legal responsibility of the company that sponsors them. That company must critically review and monitor the collection of raw data and their subsequent analysis and interpretation. The company must be concerned about its long-term reputation, as well as the threat of criminal penalties if the data are falsified in any manner. Furthermore, companies are generally not inclined to take enormous risks with investigators whose falsified or biased data might lead to a large financial loss. If the bottom line

Lewis Pell is Chairman of Vascu-Care Inc. and President of OPAC Corporation.

for a company is profit, the company must be convinced that the investigator's results are meritorious.

The second safeguard in the United States is the FDA, which conducts an exhaustive review of clinical trials. These reviews may last many months, and the FDA has a reputation for extreme rigor in its efforts to protect the public. The review of investigations by the FDA is conducted by scientists and physicians and is concluded with a critical review by a panel of clinical experts.

The third safeguard is subsequent peer review by other scientists. Disclosures of all financial ties between researchers and the products and procedures they are investigating should be made mandatory by the journals that publish the results of these investigations. Such disclosure is already requested by the FDA. It permits the reader to weigh the merits of the investigation against any possible sources of bias introduced by a researcher with a vested interest in the outcome.

It is extremely important that clinical investigators be permitted to have an economic interest in products they are evaluating. Without such incentives, a major obstacle to important medical advances might harm the public far more than would the risk of unscrupulous entrepreneurs. As part of clinical studies, investigators are often asked to do much more than merely conduct the study. They must review clinical protocols, make suggestions for product improvements, "fine tune" the product or procedure, train other scientists, present their data to FDA expert panels, and place their entire professional reputation under scrutiny. Their involvement requires a great deal of time, effort, and risk for which compensation is clearly appropriate. Would it not be considered unethical on the part of the business world to withhold compensation for these activities? Large companies provide compensation in the form of grants or consulting fees. Smaller companies, with limited funds, may provide equity to the investigator.

The activities of a clinical investigator are critical to the development, regulatory approval, and subsequent use of the product. They can best be performed by scientists who have used the product in the clinical setting and are thoroughly familiar with it. Without financial incentive, it is very likely that clinicians would be reluctant to devote so much time and effort to the development of new products, and they would certainly move on to other activities that might not benefit the public as directly. It is not the intent of this editorial to reduce the process of clinical trials to dollars and cents. The rewards familiar to all investigators upon the completion of a successful project are still inherent in clinical trials for which they are compensated. Investigators still feel the same satisfaction for the good science, for the improvement of the human condition, and for the ability to contribute meaningfully to the community at large. That they receive compensation for their efforts must be regarded as just, not shameful.

The arguments against entrepreneurial interest in investigations are philosophical, not objective. No data exist to confirm that banning financial interest in clinical investigations would improve the human lot, or conversely, to confirm that permitting a profit motive would diminish the quality of science. In my opinion, an objective look at our advances in the past decade argues against the position taken by Relman and others who would restrict potential sources of income for investigators. Who is to set the ethical standards for clinical investigators? How will the investigators respond? Before even more restrictions are placed on an already stringently regulated group of professionals, these questions should be scientifically and thoroughly researched.

References

Dobson R, Todd JS, Manuel B. (1986). Conflicts of interest and the physician entrepreneur. N Engl J Med 314:250–253.

Hyman DA, Williamson JV. (1989). Fraud and abuse: setting the limits on physicians' entrepreneurship. N Engl J Med 320:1275–1278.

Relman AS. (1980). The new medical-industrial complex. N Engl J Med 303:963–970.

Relman AS. (1984). Dealing with conflicts of interest. N Engl J Med 310:1182–1183.

Relman AS. (1985). Dealing with conflicts of interest. N Engl J Med 313:749–751.

Relman AS. (1988). Medicine as a profession and a business. In: McMurrin SM, ed. The Tanner lectures on human values. Vol. 8. Salt Lake City: The University of Utah Press, 283–313.

Relman AS. (1989). Economic incentives in clinical investigation. New Engl J Med 320:933–934.