



EVALUATING THE ADEQUACY OF DISCLOSURE AS A SOLUTION TO THE PROBLEM OF CONFLICT OF INTEREST IN BIOMEDICAL RESEARCH

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ABSTRACT

A potential risk of conflict of interest currently exists in research. The financial considerations play a greater role in the decisions that are necessary in the process of research. Traditional pharmaceutical companies began to invest, not just in the commercial development of biomedical discoveries for the marketplace, but in the research centres that could deliver the discoveries. Cooperation and interdependence between industry and research institutions is not inherently wrong, but these unions must be regulated and managed through regulatory mechanisms. When a financial relationship is been disclosed, it would be closely evaluated in order to determine the risk of an undue influence leading to bias, or loss of scientific objectivity. To sum up, a conflict of interest is a potential, but not a certain occurrence. Banning funding for university research by industry is unrealistic. The only effective way to proceed is to implement oversight and regulation that makes both industry funding entities and researchers aware that their activities will be monitored for the benefit of public safety as the more valued concern.

Key words: Conflict of interest, Disclosure, Research, Bias, Regulations

INTRODUCTION

A potential risk of conflict of interest currently exists, between the way that biomedical research is conducted in an academic setting, and increased levels of commercial funding of research. The risk that industrial, financial or other interests may improperly influence conduct of researcher and other professionals forms the root of this problem. For clinical researchers, the demands of the pharmaceutical and medical marketplace may exert an undue influence on clinical trials and other processes, through the desire of commercial interests to generate an outcome that is favourable to their interests. Oversight and regulation for transparency of influence, funding and research outcome is needed to offset these concerns. These concerns emerged with the passage of Bayh-Dole Act in December 1980 (Emanuel and Thompson 2008: p. 758). The Act granted U.S. universities and non-profit organizations the right to claim control over intellectual property in the form of inventions and other discoveries, even if such inventions and discoveries had been the result clinical research supported by federal funding. One result of the Act was that the pharmaceutical industry and other commercial entities began to seek increased involvement in clinical research conducted at research institutions such as universities (Emanuel and Thompson 2008). Correspondingly, commercial considerations also began to play a greater role in the decisions that are necessary in the process of research.

Another related outcome has been an increase in the number and application of regulations that are designed to inhibit potential conflicts between commercial interests and the goals of research, which include academic freedom and objective scientific inquiry. Yet significant uncertainty remains, about what may constitute a conflict of interest, how conflicts should be managed, and which standards should be used as the basis for regulation.

Brief History

In 1970s, scientific advancements in the ability to use recombinant technologies to splice human DNA and create microorganisms in the laboratory, led to the establishment of the biotechnology industry (Emanuel and Thompson 2008). These advancements presented researchers with the potential for significant financial gain from their discoveries, and with this possibility, the potential conflicts of interest in biomedical research began to escalate in scope. For example, biotechnology companies

such as Genentech and Biogen were both founded by academic researchers seeking to commercialize the scientific innovations that they had participated in developing (Emanuel and Thompson 2008).

A connection between industry and academia began to develop that was stronger than had previously existed. Traditional pharmaceutical companies began to invest, not just in the commercial development of biomedical discoveries for the marketplace, but in the research centres that could deliver the discoveries. These included university research programs; the companies donated large amounts of money to academic institutions, with the stated expectation of gaining the right to turn future discoveries into profitable commercial ventures (Emanuel and Thompson 2008).

The funding of research programs advanced in 1974 when Harvard Medical School entered into a \$23 million agreement extending over 12 years with Monsanto, to fund clinical research of antiangiogenesis factors (Emanuel and Thompson 2008). In exchange for the funding, Monsanto received exclusive worldwide licensing rights for all inventions that might emerge as a result of the research. Soon after the Monsanto agreement, Harvard Medical School signed another agreement with DuPont, which involved \$5 million in funding for a new genetics department (Emanuel and Thompson 2008).

In 1980, Hoechst AG followed the example of Monsanto by entering into an agreement to donate tens of millions of dollars over a period of ten years to fund the Department of Molecular Genetics at Massachusetts General Hospital (Emanuel and Thompson 2008). In exchange, the company would receive the exclusive rights to licenses for all commercially valuable discoveries. The Bayh-Dole Act of 1980 accelerated this trend, by trend by stimulating an increase in collaboration between universities and private industry. As the rate of agreements between universities and industry rose, the balance of sources for research funding shifted. Prior to the Bayh-Dole Act, more than half of all university research funding for biomedical had come from the federal government. After the Act, more than half of this funding began to come from private industry (Emanuel and Thompson 2008).

The Conflict of Interest

As the rate of funding from private industry increased, attempts were made to limit conflicts of interest in research at universities. Shortly after the founding of biotechnology companies such as Genentech and Biogen in the early 1980s, the state of California began to require that professors at state-funded colleges and universities disclose any financial interest in companies affiliated with research in which they were involved (Emanuel and Thompson 2008).

In 1988, a research scandal illustrating the dangers of corporate funding and biomedical research arose. An ophthalmology fellow at the Harvard-affiliated Massachusetts Eye and Ear Infirmary developed a vitamin A-based ointment that was designed to alleviate dry eye syndrome (Emanuel and Thompson 2008). Dry eye syndrome is a painful condition, in which the eye is unable to maintain a tear film. When preliminary testing appeared to indicate that the ointment was efficacious and safe, the fellow, who was named Tseng, sold the rights for the treatment to a pharmaceutical company for \$310,000. In addition, Tseng had purchased 530,000 shares in the pharmaceutical company. Also, Tseng's senior research advisor at Massachusetts Eye and Ear Infirmary also owned shares in the company, while at the same time, participating in research development of the treatment (Emanuel and Thompson 2008).

It was later revealed that the clinical trials for the ointment were redirected numerous times, in order to satisfy the commercial interest of bringing the ointment to market, rather than for valid scientific reasons. Although the original testing protocol had specified trials on 50 patients, the study group was increased to 250 participants (Emanuel and Thompson 2008). The pharmaceutical company had succeeded in obtaining orphan status for the drug, and then sold stock in the drug to the public. Tseng had already sold his shares in the company at a substantial profit, when research began to demonstrate that the ointment was no more effective than a placebo. The study on the ointment was stopped, and an investigation began. Although subsequent investigation found that no patients had been harmed, and no specific scientific misconduct was uncovered, the dangers of linking research to financial gain for researchers had become clear (Emanuel and Thompson 2008).

The Disclosure

By the mid-1980s, leading general medical journals established the practice of requiring authors to disclose potential financial conflicts of interest in published research. In 1985, *New England Journal*

of Medicine began to include disclosure on the sources of funding for published studies, including “direct business associations by a corporation that has financial interest in the work being reported” (Emanuel and Thompson 2008: p.759). The *Journal* requested that researchers voluntarily give a statement of financial interest to its editors who then made decision to include the information as a part of the published articles. This was followed in 1988 by a policy of the International Committee of Medical Journal Editors requesting that authors voluntarily disclose any financial affiliations with the research submitted for publication in professional publications. By the mid-1990s the biomedical research community had established new rules requiring disclosure, and some professional societies also required officers and researchers to disclose financial interests as part of published research (Emanuel and Thompson 2008).

The death of a patient or study subject represented the strongest indication of the potential abuse of research. In September 1999, Jesse Gelsinger, an 18-year-old male who had participated as a study subject in an experimental gene transfer project at the University of Pennsylvania died. This was the first death that could be directly attributed to gene transfer experimentation. In the ensuing investigation, an avalanche of evidence revealed negligence in the informed consent process for Gelsinger (Emanuel and Thompson 2008). It was also revealed that the University of Pennsylvania had failed to clearly disclose animal data on the toxicity of the gene transfer process, as well as toxic side effects that had occurred with previous study subjects. The University should have suspended or closed the study, but proceeded out of financial motives for the potential future gain.

Yet “Universities do not come to the task [of controlling conflict of interest] with entirely clean hands, for they, too, may have financial interests that could conceivably bias the results” (Emanuel and Thompson 2008: p. 762). For instance, universities have often formed consortia with the goal of bidding for contracts for prospective drugs. Columbia and Duke are examples of two universities that have established consortia, not for the purpose of supporting clinical research, but with the goal of generating monetary return (Emanuel and Thompson 2008). When universities expect to benefit from these enterprises, they have a large stake in sustaining relationships by generating positive results for the product testing; “To that extent, they have an incentive to avoid results that will disappoint their corporate sponsors” (Emanuel and Thompson 2008).

Cooperation and interdependence between industry and research institutions is not inherently wrong, but these unions must be regulated and managed through regulatory mechanisms. The “deep malaise in research universities is not likely to be resolved adequately through the kind of risk management strategies” (Schafer 2004). Some critics have proposed that the core university values of scientific research integrity and academic freedom are threatened by commercial funding of research (Schafer 2004). Mere disclosure of conflicts of interest and regulation of agreements for funding between researchers and industry not likely to be adequate, Schafer (2004) has asserted. “Instead, there needs to be something close to an outright prohibition on the much vaunted ‘partnerships’ between university researchers, on the one hand, and the pharmaceutical industry, on the other” (Schafer 2004).

The norms of research science have been transformed through increasingly close dependency of the research universities on funding originating in the corporate world. Funding gained from corporate sponsorship has the potential to bias the results of clinical drug trials, and compromise the principles of academic freedom and scientific objectivity (Schafer 2004). Two different strategies have been proposed for mitigating these risks: the regulatory approach, which proposes managing the risks of accepting industry funding for university research, and the more radical approach, of sequestration involving the complete elimination of corporate funding for biomedical research (Schafer 2004).

While Schafer (2004) has asserted that complete disallowance of corporate funding is the only way to assure that academic standards for research are maintained, a more realistic approach necessitates mechanisms for full disclosure and oversight of potential conflicts of interest. In this model, all researchers would be governed by an institution’s disclosure policies. The institution would maintain a conflict of interest committee or equivalent, which would be made aware of any situations in which a researcher maintains a stake in the results of the research.

When a financial relationship is been disclosed, it would be closely evaluated in order to determine the risk of an undue influence leading to bias, or loss of scientific objectivity. The committee may conclude that additional safeguards are necessary (Lo and Field 2009). These safeguards could

consist of a risk management plan in which a researcher without a conflict of interest is included as a participant in the research, as well as disclosure of the conflict to co-investigators, and in presentations or publications of the research conclusions.

The possibility of conflict of interest can be expected to persist at the institutional level, in which research or proposed research by a university or medical school is related to a financial interest, such as a patent or start-up company. At times, an individual participant in research may represent a definite conflict of interest, while being essential to the completion of research. An example: participation in a clinical study by the inventor of a medical device requiring implantation by a complex surgical procedure that no one else has the ability to implement (Lo and Field 2009).

CONCLUSION

A conflict of interest is a potential, but not a certain occurrence. Research investigators may have to be trained in understanding of conflict of interest, so such conflicts may not burden “socially valuable collaborations between academic researchers and industry” (Lo and Field 2009). The potential exists for biomedical research to generate products and procedures that can only emerge through close partnership between research institutions and industry. Banning funding for university research by industry is unrealistic. The only effective way to proceed is to implement oversight and regulation that makes both industry funding entities and researchers aware that their activities will be monitored for the benefit of public safety as the more valued concern.

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