Symposium

Relationships with Industry: Critical for New Technology or an Unnecessary Evil?*

By Joshua J. Jacobs, MD, Moderator, Jorge O. Galante, MD, DMSc, Sohail K. Mirza, MD, MPH, and Thomas Zdeblick, MD

Recently, our profession has been subject to an unprecedented amount of scrutiny in the lay press concerning our professional ethics, specifically with regard to our relationship with the orthopaedic industrial sector. On March 31, 2005, the Wall Street Journal, New York Times, USA Today, and other newspapers ran major stories on the United States Department of Justice's subpoenas to several large orthopaedic device manufacturers concerning their relationships with orthopaedic surgeons.1-3

This issue, of course, is not unique to orthopaedic surgeons. In fact, the entire medical profession is under scrutiny. The former editor of the New England Journal of Medicine, Dr. Jerome Kassirer, in his book entitled On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health, stated that "financial conflicts of interest threaten patient care, taint medical information, and raise costs. They create deception, impair physicians' judgment, and reduce their willingness to be their patients' advocates. They reduce professional dignity and integrity, denigrate the profession, and erode trust in the profession's practitioners, researchers and institutions." In addition, Dr. Kassirer recommended a 10-point "roadmap" with what some would consider draconian solutions to this "crisis."

Is our profession tainted? Do we need to adopt draconian policies in order to prevent financial conflicts of interest from influencing our patient care and research activities? As a group of leaders of our profession, the American Orthopaedic Association tackled these questions at its 2005 annual meeting in order to promote an open dialogue and develop strategies to maintain the high ethical standards of our profession while still fostering innovation and improvements in patient care. This paper presented at the Annual Meeting of the American Orthopaedic Association, Huntington Beach, California, June 24, 2005.
summarizes the proceedings of this symposium in a debate-type format. A practical approach to managing financial conflicts of interest, particularly with regard to clinical research, is also presented.

**Pro Position**

Interactions with Industry: Facing Reality

**BY JORGE O. GALANTE, MD, DMSC**

Interactions with industry are commonplace in all branches of medicine. These interactions have had a fundamental and widespread impact on all of the advances in the medical sciences for the last few decades. The potential benefits of these relations are undeniable; they are relevant to the patients who constitute the ultimate beneficiaries, to the medical profession at large, to the academic entities, and without a question to industry. It is my role to emphasize the positive aspects of these interactions. However, conflicts of interest can arise in many different ways and I will address them as well.

Orthopaedic surgery is no different from any other surgical or medical specialty when dealing with the subject of interactions with industry. As a specialty, orthopaedics is very involved with joint prostheses, spinal surgery implants, and internal fixation devices and, as a result, a multibillion dollar industry has spawned with worldwide reach. However, the field of orthopaedics is much broader and involves many interactions with the pharmaceutical industry, such as work in the areas of deep-vein thrombosis and its prevention, osteoporosis, and anti-inflammatory medications. Contemporary issues, such as tissue engineering, robotic surgery, and the eventual introduction of growth factors into the various facets of clinical practice, make the interactions with the biotechnical industry critical for the success of future developments.

What is the nature of these interactions? They range over a broad number of issues and include support of research by means of contracts or grants, licensure agreements to manufacture a product, consulting agreements, membership of physicians in advisory boards, equity ownership by the physician or the parent institution in the industrial outfit or more frequently in start-up companies, support of continuing medical education activities, independent offers of instructional opportunities, gifts, physicians acting as expert witnesses in industry-related civil suits, and others.

How frequent are these interactions? It is difficult to assess the incidence of these types of events in relation to the orthopaedic surgeon in private practice. Some form of interaction occurs almost on a daily basis through contacts with industry representatives and salesmen in the office or in the operating-room environment. It is easier, though, to establish some measure of quantity when looking at clinicians or investigators working in an academic environment. A wide range of financial interactions between academic institutions, investigators, and industry at large clearly exists and has been well documented. Studies have suggested that 23% to 28% of academic investigators in biomedical research have received research funding from industry and that up to one-third of the investigators at academic institutions had personal financial ties with industry sponsors.

The magnitude of these interactions is not the product of chance alone. Partly, it is the result of governmental policies designed to facilitate the transfer of technology to the marketplace. In 1980, Congress passed the Bayh-Dole Act, which allowed non-governmental organizations to control patents on inventions developed with federal funds. Before that, the federal government held the intellectual property rights to any inventions that were developed with federal funds, and it allowed inventions to be used freely. Over the ensuing years, the number of patents that universities filed in the medical sciences grew markedly, as did the number of licensing agreements with industrial firms. While at one time governmental policies may have had a major impact in fostering these collaborations, today the benefits that accrue to each one of the parties involved are such that these interactions continue to grow and thrive.

We are faced with two relevant questions: are these interactions valuable and are they appropriate? The question related to value is one that can easily be answered. Interaction with industry is the basis for technology transfer. Industry plays a key role in essentially every aspect of orthopaedic clinical practice and is an intrinsic partner with medicine in providing the tools that the practitioner needs to serve the needs of his patients. It is also the key to the future developments that are rapidly changing the nature of orthopaedic surgery. The question about appropriateness leads us head-on to the concept of conflicts of interest. These fundamental issues of ethical behavior are intimately tied to the character of individual physicians.

I would like to focus on these issues as they relate to a subject with which I have become familiar through my own involvement over the past thirty-five years. It is the field of total joint prostheses and the interactions that take place with industry in relation to research and development activities associated with the introduction of prosthetic devices to the marketplace as well as the evaluation and reporting of relevant clinical results.

In a very simplistic model, an idea is first conceived by an investigator and leads to the formulation of a hypothesis. This idea could be the development of a new material for biological fixation, a design concept for a prosthetic device, a wear-resistant articular surface, or a number of other issues relevant to prosthetic design. In the appropriate academic environment, the validation of the hypothesis leads to a research program that could be a series of animal or laboratory in vitro experiments, mechanical tests, cadaver studies, gait studies, or computer validations, depending on the nature of the subject.

At some point in this process, it may become obvious that the project
has valuable practical applications and that the eventual outcome will be its incorporation in a prosthetic device. The idea is an original creation; in other terms, it is an invention. As such, it is subject to the principles of intellectual property and thus worthy of considering for a patent.

Intellectual property is a concept basic to the financial structure of our society and to the functioning of our economy. Since 1790, the United States government has awarded patents to encourage innovation by granting inventors the right to prevent others from making, using, or selling their inventions for a limited period of time. The protection afforded by the patent is critical for the involvement of industry. At this juncture, researchers typically discover that they cannot advance the project further, partnerships with industrial firms ensue, and a license agreement is concluded. The next step is the assembling of the development team, which includes the members of the industrial firm who will work with the investigators and clinicians in the design of the device and all of the other elements necessary to bring it to the marketplace.

In the past, the division of responsibilities was clear. The investigator generated the fundamental knowledge that industry in turn developed and marketed. However, the orthopaedic industry has changed and evolved dramatically over the last two decades. Most companies have sophisticated research capabilities headed by individuals trained in academia. Thus, beyond product development, manufacturing, and marketing, industrial firms are also engaged in research and bring relevant information to the mix.

The development team addresses the design of the device, but that is only part of the process. Clinicians are indispensable in refining and standardizing surgical techniques and indications and in anticipating and avoiding potential problems. This can lead to substantial improvements in outcomes. Clinicians are also important in the design of the educational activities that will be needed to train and educate surgeons, operating-room personnel, and others in the proper use of the prosthetic device. They may also be involved in the clinical trials required for eventual regulatory approval of the device. At some point, the device will be approved by the regulatory agencies and will enter the marketplace. This is where conflicts of interest become apparent in all of the areas mentioned above.

As a result of the license agreement, royalties will flow. Many such agreements base the royalties on a given percentage of sales, and the flow of money could be considerable. Part of the money may be used to further fund the research operation, or for other departmental or institutional purposes. In the cases of successful patents, institutions have derived substantial sums from these types of sources. In most cases, the investigators or developers of the device also receive some portion of the royalties. Will the financial benefits that are accruing to both the investigator and the institution modify their behavior and introduce an element of bias in their decisions to the detriment of patients and of society at large?

The developer participates in a number of activities designed to implement the introduction of the device to the marketplace in a safe and reproducible manner. Presentations at meetings and lectures and the publication of clinical research results in orthopaedic journals are the usual venues where the experience with the device is presented. The potential for bias, whether induced by scientific ego factors or by the associated financial incentives, is an issue of major concern in all of these settings.

There is a voluminous amount of literature on the subject of conflicts of interest and on the methods to resolve them. The issue of bias is also well documented. In a comprehensive review on the impact of industry interactions on published biomedical literature, an important association was shown between industry sponsorship and pro-industry conclusions. Industry sponsorship was also associated with restrictions on publication and data-sharing. In a recent review of randomized clinical trials, it was found that industry-funded trials were more likely to be associated with pro-industry findings, both in medical trials and surgical interventions.

The appearance of bias may not always be the product of dishonesty. It is not uncommon for the developers of a device or surgical procedure to have better results than other surgeons simply because they are more familiar with the relevant principles and surgical technique. However, intellectual honesty and ethical character are two critical qualities that are not universally present. They can only be exercised by the individual physician and are difficult or impossible to legislate.

There are many policies designed to deal with conflicts of interest. The American Medical Association, the American Academy of Orthopaedic Surgeons, individual academic institutions, scientific journals, and the federal government all have specific guidelines. Industry has developed policies to address these issues as well. All of these policies and documents set up a framework that should have the capacity to prevent or resolve most conflicts of interest. However, from a practical viewpoint, problems still arise with disturbing frequency.

The orthopaedic industry has grown and evolved over the past two or three decades and has developed very sophisticated biotechnical capabilities. No one can deny that this industry has played a key role in important advances in patient care. However, the ultimate fiduciary responsibility of industry is not to patients but to stockholders. Profit is the driving force. Thus, in parallel with their research and manufacturing capabilities, industrial firms have developed sophisticated and aggressive marketing departments and expertise—witness the introduction of direct marketing of orthopaedic implants to patients. A variety of interactions in which marketing plays the major role have developed between orthopaedic surgeons and industry.

I would like to distinguish among
several types of interactions (Table I). There are those that involve intellectual property (Type 1), those that consist of consulting agreements in which the surgeon addresses a specific issue (Type 2), those that are designed primarily to use the orthopaedic surgeon as a marketing tool (Type 3), and those that are intended to provide a financial benefit to the surgeon in exchange for the use of a device (Type 4). When intellectual property is involved (a Type-1 interaction), as described previously, marketing is not the driving force. There is, however, an undeniable marketing value when an opinion leader lectures about a device he has developed or, for that matter, speaks in public on an unrelated subject although promotion is not the purpose of the exercise. The same holds true when a legitimate consulting agreement is in place (a Type-2 interaction).

On the other hand, when the surgeon is paid to promote a device without having contributed in any manner to its existence (a Type-3 interaction), the picture is different. These Type-3 interactions are common practice today. As with a consulting agreement, the remuneration should be related to the magnitude of the effort invested and not go beyond that. The situation that is most disturbing is the Type-4 interaction, in which the physician is benefiting financially in exchange for the use of a device. A company, in an effort to increase business, may pay surgeons who actually do not provide services that justify that compensation. This issue is probably at the heart of a recent probe by the Department of Justice into makers of orthopaedic devices vis-à-vis their relationships with the orthopaedic surgeons who consult for them. Although the process has just begun, it would be desirable for this investigation to result in a solution to the problem of nonethical conduct of both industry and orthopaedic surgeons without interfering with the valuable aspects of the industry-surgeon interaction. The ideal model should be one that allows productive collaborations without the hint of real or perceived misconduct.

In conclusion, interactions with industry are crucial to the future of orthopaedic surgery. Conflicts of interest that arise must be managed by the zealous application of the appropriate ethical practices from both the surgeon and industry. A critical review of marketing procedures and the strategies that are used to promote the utilization of the manufacturer’s products should resolve many of these difficult issues.

**CON Position**

**Perception Is Reality: Damaging Effects of Financial Conflicts of Interest on Public Trust in Orthopaedic Surgeons**

BY SOHAIL K. MIRZA, MD, MPH

“When the orthopedist says you need surgery and you are in terrible pain, you assume he is right. . . . Think long and hard,” advised a sixty-five-year-old minister who had undergone three spinal fusion operations without a reduction in back pain.

Public trust in the medical profession is being challenged by accounts of financial motives contaminating the judgment of physicians. Surgeries are particularly at risk for damage from this charge since they frequently are also innovators of new surgical techniques and inventors of new devices. The surgical literature, compared with that of other medical disciplines, lags in creating a strong evidence-based foundation for practice, and much of the surgical care today depends on the experience and judgment of surgeons. In the face of uncertain science, patients largely trust this judgment, assuming that surgeons place the interests of patients first and foremost, beyond personal gain. This trust charges surgeons with great responsibility to protect the integrity of their surgical practice and clinical research.

Judgment, even under the best intentions, is susceptible to influence from many factors. Among the most damaging of these factors are perceptions of personal financial gain by the decision maker, such as accusations of performing surgery for lucrative reimbursements or demanding kickbacks from orthopaedic device manufacturers in exchange for using their devices. These serious charges of financial conflicts interfering with surgical judgment have led to investigation by the Department of Justice into the relationships between orthopaedic surgeons and the device industry. Orthopaedic surgeons need to reevaluate their relationships with device manufacturers and address concerns about the influence of financial conflicts of interest.

**The Nature of the Conflict**

The values endangered by conflicts of interest in medicine are the core values that define science, medicine, and industry. Science is founded on inquisitiveness, objectivity, candor, and openness. Hidden conflicts of interest create concerns of interference with judgment and violation of public trust. In medicine, doctors take an oath to place the interests of each individual patient above their self-interest. It is a public declaration of a personal commitment. Enforcement is internal, by the individual’s conscience. Disclosure of contrary influences is voluntary. Penalties of violating the oath are invisible. In industry, business managers have a fiduciary duty to the business owners. They are hired to protect the interests of the shareholders. Performance is publicly measured by concrete financial metrics. Time frames of evaluation are
short. Good performance is generously rewarded. Poor performance is reprimanded sternly, often with replacement of the leadership.

These divergent allegiances of scientists to the public, doctors to patients, and managers to owners create the context for a growing debate on the role of financial conflicts of interest in medicine. The extent of the debate is reflected in nearly 1000 articles published on this topic during 2003 and 2004 (Fig. 1). The seriousness of the debate and the high stakes of its consequences are evident in the fact that most have been published in the most respected publications in medicine, including the British Medical Journal, the New England Journal of Medicine, and the Journal of the American Medical Association (Fig. 2).

Terminology of Conflicts of Interest
The responses to conflicts of interest are often distorted by misconceptions and careless use of terms. Conflict of interest does not equate to bias. Conflict of interest simply means “a conflict between one’s obligation to the public good and one’s self-interest.” Bias, in general usage, means “partiality, a mental leaning or inclination.” In research, bias refers to unintentional systematic or nonrandom error. Having a conflict of interest does not imply a moral or ethical failing; problems arise when undisclosed conflicts lead to bias. Some
conflicts of interest arise from universal motives among academic investigators, such as the desire for career advancement, recognition, and contribution of new knowledge. These intrinsic conflicts of interest are fundamental to the research endeavor. They are rarely discussed or disclosed, and they are impossible to prohibit or regulate.

The biasing effect of conflict of interest is commonly perceived as a matter of deliberate choice. However, social science research shows that self-interest leads to bias that may be unintentional, unconscious, and unavoidable. Self-interest distorts how individuals unconsciously weigh arguments and make choices when they have a stake in the outcomes. It affects choices indirectly. Even when individuals are explicitly instructed about bias, motivated to remain impartial, and aware that it is in their best interest to remain impartial, still they tend to deny bias, yet succumb to it.

The Role of Industry Funding in Medical Research

Partnership between medicine and industry is the foundation of translational research and technology transfer envisioned in the Patent and Trademark Law Amendment Act, also known as the Bayh-Dole Act of 1980, which allowed universities to receive patents on research funded by the federal government. This type of research has been reemphasized in the National Institutes of Health Roadmap for Medical Research. Innovators and developers usually know the most about their inventions, so they are well suited to study them. Furthermore, inventors and innovators deserve recognition for their contributions.

Industry benefits from collaboration with academic researchers. A 1994 survey of senior executives in 220 life-sciences companies showed that 92% had relationships with academic institutions; 62% secured patents, 64% marketed products, and 61% obtained sales revenue at least in part because of their university-based research.

Physician-researchers face challenging competition to secure research funding, and industrial research contracts provide an alternative to federal grant mechanisms. In comparison with the federal support for biomedical research of $25 billion and the private foundation support of $8 billion to $10 billion, industry research and development investment in 2000 was estimated to be $55 billion to $60 billion. A 1994 survey of 2052 faculty members reported that 28% received research support from industry. Orthopaedic surgeons studying devices face additional challenges since federal grant support is unlikely for research on commercial devices. In the orthopaedic literature, up to 75% of clinical studies on total hip arthroplasty and half of all publications and presentations on adult lower-extremity research are commercially sponsored.

Industrial funding, however, differs from federal funding. It can reduce research quality and investigator autonomy. It is more likely to have inactive control groups, a higher dose of the test drug, and lower methodological quality. Industry-sponsored researchers are also more likely to report delays in the publication of their research results and report denial of access to some results. These general observations create perceptions of bias in industry-funded research. Perceptions of bias are particularly difficult to dispel when investigators conducting safety and efficacy evaluations of specific devices...
develop relationships with the device manufacturer involving personal gain (Fig. 4). Yet, these types of arrangements are common. A systematic review found that 43% of medical researchers receive research-related gifts, and 33% have personal financial ties with the sponsor of their research.

Research Subjects in Industry-Funded Research
The effects of treatment in clinical research are typically modest, the definition of success and failure depends to a large extent on judgment, and the safety of human subjects is in the hands of the investigator. In orthopaedic clinical trials, the perception of conflict of interest can be especially damaging, even when the benefits for patients, researchers, and sponsors may be perfectly aligned. The simplified view in the eyes of the public is that “. . . in the world of medical devices . . . inventors are researchers. Researchers are promoters. Promoters are investors. And, finishing the circle, investors are inventors.”

Research subjects want disclosure of financial conflicts for investigators and institutions. In a survey of 5478 potential research participants, 87% felt financial conflicts of interest should be disclosed as part of informed consent, with most respondents valuing this information as “extremely” or “very” important. When some research patients suffer adverse outcomes, failure of this disclosure can become front-page newspaper headlines. The damage from the perception of impropriety has lasting effects, even if in the end the physicians are cleared of wrongdoing.

Institutional Policies for Relationships Between Academia and Industry
Institutional policies governing industry relationships have varied widely in specifying the types of interests that must be disclosed, the persons who must disclose them, the party to which disclosure must be made, and the types of interests that are prohibited. Research subjects want disclosure of financial conflicts for investigators and institutions. In a survey of 5478 potential research participants, 87% felt financial conflicts of interest should be disclosed as part of informed consent, with most respondents valuing this information as “extremely” or “very” important. When some research patients suffer adverse outcomes, failure of this disclosure can become front-page newspaper headlines. The damage from the perception of impropriety has lasting effects, even if in the end the physicians are cleared of wrongdoing.

Institutional Policies for Relationships Between Academia and Industry
Institutional policies governing industry relationships have varied widely in specifying the types of interests that must be disclosed, the persons who must disclose them, the party to which disclosure must be made, and the types of interests that are prohibited (Table II). Of the ten medical schools receiving the most federal research funding in 2000, only one had a policy prohibiting clinical researchers from personal financial interests, such as holding stock, stock options, consulting agreements, or decision-making positions in a company that may appear to be affected by the results of their research. An analysis of the policies from eighty-nine of the 100 institutions in the United States receiving the most funding from the National Institutes of Health showed that most policies lacked specificity in prohibiting between researchers and institutions. The International Committee of Medical Journal Editors (ICMJE) has revised its “Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication,” holding investigators accountable for the design and conduct of clinical trials. The ICMJE hopes to protect the integrity of the research process by requiring that investigators retain access to all trial data, control all editorial and publication decisions, and fully disclose the role of the sponsor.

Since these surveys were done, the Association of American Medical Colleges (AAMC) has recommended general safeguards for managing ties between academic institutions and industry. The AAMC guidelines prescribe any financial interest on the part of the investigator of a drug, but they are ambiguous about devices and are silent about basic, nonclinical research. The International Committee of Medical Journal Editors (ICMJE) has revised its “Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication,” holding investigators accountable for the design and conduct of clinical trials. The ICMJE hopes to protect the integrity of the research process by requiring that investigators retain access to all trial data, control all editorial and publication decisions, and fully disclose the role of the sponsor.
However, research agreements between medical schools and industry sponsors routinely fail to adhere to ICMJE requirements.

In contrast to the concerns of research subjects, institutional policies rarely require disclosure of financial conflicts of interest to research subjects. In a review of conflict-of-interest policies at 235 medical schools and other research institutions that received more than $5 million in federal grants in 1998, only three institutions (1%) required disclosure of conflicts to research subjects. Even when institutions have detailed and explicit policies, investigators are often poorly informed about them. Although most investigators acknowledge the risk posed by conflicts of interest for others and affirm the need for policies and regulation, many believe that these risks do not apply to them. They believe that they can recognize conflicts, avoid bias, and regulate their own behavior.

### Interpretation of Results in Industry-Sponsored Research

Industry sponsorship of research leads to the publication of results that are favorable to the sponsor (odds ratio, 3.60; 95% confidence interval, 2.63 to 4.91). This effect may be due to a biased interpretation of the results. In an analysis that adjusted for treatment effect and adverse events, trials funded by for-profit organizations were more likely to recommend the experimental drug as the treatment of choice compared with trials funded by nonprofit organizations (odds ratio, 5.3; 95% confidence interval, 2.0 to 14.4). The association between industrial funding and pro-industry results has been even stronger for surgical trials (odds ratio, 8.0; 95% confidence interval, 1.1 to 53.2). A similar association has been observed in orthopaedic research publications, in which 78.9% of industry-funded studies described a positive outcome compared with 63.3% of non-funded studies.

Similarly, in spine research, 73% of the sponsored studies showed favorable results compared with 44% of nonindustry-funded studies (odds ratio, 3.3; 95% confidence interval, 2.4 to 4.5). The differences are more substantial in joint arthroplasty studies. In one analysis, 93% of the total hip arthroplasty studies funded by implant manufacturers showed favorable results in comparison with 37% of the independently funded studies. For knee arthroplasty, 75% of the studies funded by industry reported favorable results compared with 20% of the independently funded studies. Furthermore, surgeons reporting on hip and knee arthroplasty performed with devices for which they received royalties noted no negative outcomes related to their devices.

### Policies of Scientific Journals on Industry Funding

Scientific journals have not developed consensus regarding methods and ter-
minologies for disclosing conflicts of interest. The New England Journal of Medicine, in 1984, was the first medical journal to require authors to disclose financial conflicts of interest\(^7\). In 1997, only 220 (15.8%) of 1396 highly ranked biomedical and scientific journals had conflict-of-interest policies\(^2\). Among the journals with established disclosure polices, only one (0.5%) identified authors as having personal financial interests in the subject of their research. A majority (65.7%) of the journals with disclosure policies reported no disclosures for any articles. Given the estimated prevalence of financial conflicts for 28% of the academic investigators\(^1\) and 34% of the biomedical publications\(^1\), the low disclosure rates suggest problems with compliance, some of which may be attributed to interpretation of the terms and conditions of disclosure policies\(^4\).

Editorials and review articles may be especially vulnerable to author bias. In a study of review articles on the passive effects of smoking, positions favorable to industry were advocated by 94% of the articles written by authors affiliated with the industry compared with 13% of those written by authors without such affiliations\(^3\). The New England Journal of Medicine uniquely excluded editorials written by individuals with financial ties to the issues they discussed, but it acknowledged difficulties in finding disinterested editorialists to write about drug and device studies\(^4\) and admitted failures in enforcing its conflict-of-interest policy\(^5\). Ultimately, the authorship policy had to be relaxed, although disclosure policies remained strong\(^6\). Other journals have been criticized for lax policies\(^6\). More recently, the International Committee of Medical Journal Editors has revised its policy on investigator accountability in industry-sponsored research\(^7\).

**Disclosure of Financial Conflicts of Interest**

The purpose of the disclosure of conflicts of interest is to allow the recipients of information to discount the provided information by some amount, based on the type and extent of the conflict of interest. Recipients, however, may not know how much to discount the findings due to disclosed conflicts, even if the disclosure is clear and comprehensive\(^8\). Ambiguous or incomplete disclosure further limits clear valuation of the evidence. Disclosure policies vary with regard to identifying the amount of financial interest at which disclosure is required and identifying to whom disclosure is required\(^8\). This variation makes it difficult for investigators to know when and what to disclose\(^8\). Terms are often not defined, serious conflicts are neglected, and entities external to the institution to which disclosure must be made are not identified\(^8\).

In 1998, only sixteen (7%) of 235 medical schools and research institutions receiving federal funding had conflict-of-interest policies that required disclosure to journals, and only twenty (42%) of the forty-eight highest-ranked journals required authors to disclose conflicts of interest\(^1\). In interviews of thirty-four randomly selected clinical researchers at two institutions, 58% inaccurately described their institution's conflict-of-interest policy and 20% had only partial understanding of the policy\(^1\).

The concept for setting thresholds for disclosure assumes that the size of the gift determines its potential to influence the recipient and that, below some threshold, smaller gifts have no influence. A review of the effects of gifts on behavior showed flaws in this assumption\(^2\). Gifts, regardless of size, solicited or unsolicited, engender feelings of indebtedness and obligation, and they compel the recipient to reciprocate\(^2\). The obligation to repay is powerful and can unconsciously influence judgment and behavior, even for small, seemingly trivial, unsolicited gifts from disliked or distrusted people\(^2\).

**Recommendations**

The trust in surgeons and the integrity of surgical science are severely challenged by perceptions of the profession being driven by financial incentives rather than the well-being of patients\(^2\). Surgeon-scientists and device manufac-

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**A Sensible Solution**

Relationships with Industry: Eliminate Bias, Not Progress

By Thomas A. Zdeblick, MD

There is no question that, in the year 2005, the topic of medical conflict of interest turned into a heated debate. Al-
though conflict of interest in medicine is not a new concept, public scrutiny is at an all-time high.\textsuperscript{12,46,61} There are a number of reasons for this. As health care has gotten more expensive and consumes a larger percentage of our gross national product, increased scrutiny by the media has become popular. With the increasing competition for health-care dollars, any field with rapidly increasing costs presents fair game for the media. Orthopaedic surgical implants, in particular spinal implants, have come under attack. Some journalists have attributed this increase in the cost of implants to surgeon bias and profiteering.\textsuperscript{16,20,36}

Universities in general have a heightened awareness of conflict of interest. In our increasingly legalized society, many universities, fearful of litigation, have become much more stringent in their application of conflict-of-interest rules to their faculty. Much of this is driven by the aversion to adverse publicity within large universities. This can, however, be at odds with the desire of universities to maintain faculty of high reputation who live on the cutting edge of consultancy.

Equally at fault, however, is the increasing influence of industry in medical decision-making. The pharmaceutical industry as well as the surgical implant industry have increased dramatically in terms of both dollar amounts and profitability. Many of these now multinational corporations have huge research budgets and high development costs. This financial pressure makes the timely delivery of a product to market important. The drive for profit in these industries, however, also has influence on individual physician decision-making. The fine line between implant sales support and outright salesmanship and profiteering is often crossed. Particularly in orthopaedic surgery, where surgical implants are a daily fact of life, a relationship with industry is not only necessary but increasingly important for information dissemination.\textsuperscript{10,29,65}

In spine surgery, a new and more active United States Food and Drug Administration has highlighted the relationship between surgeons and industry. With the rapid innovation in implants and devices, the Food and Drug Administration approval of Investigational Device Exemption clinical trials is necessary. With Investigational Device Exemption clinical trials, the Food and Drug Administration is now actively involved in determining randomization schemes, measurable outcomes, and definitions of success. The design of these trials requires knowledgeable advice from surgeons. The sponsoring companies also require surgeons who are trustworthy to complete such trials. Most implant companies are reluctant to invite surgeons to participate in the Food and Drug Administration trials unless these surgeons are well known to the company.

Finally, much of our traditional decision-making in medicine is being called into question. Despite rational approaches to traditional treatments, it is easy for critics to call into question time-honored treatments not supported by high-quality evidence. However, the very nature of surgical decision-making often precludes obtaining the highest-quality evidence generated by randomized double-blinded clinical trials.

It is imperative that the leadership in orthopaedic surgery takes an active role in delineating appropriate guidelines for relationships with industry. The perception of bias that is currently popular among the media should not be allowed to grow unchallenged. The more rational the approach that we as leaders in orthopaedics can develop, the more effectively we will regain the trust of the public and of our patients.

**Options in Management**

Can conflicts of interest be completely eliminated? The answer is clearly no. Ties to industry are essential for the development of the surgical implants that have propelled orthopaedic surgery into the twenty-first century. Gone are the days when inventions created in a basement workshop were implanted in patients. The huge costs associated with Food and Drug Administration clinical trials and product liability defense mandate that the orthopaedic implant industry take the lead in product development. Orthopaedic surgery is uniquely connected to the implant industry. A vast majority of surgical procedures performed by orthopaedic surgeons involve the placement of an implant. For implant improvements to occur, surgeon feedback is essential. As opposed to the pharmaceutical industry, surgical device companies need to have surgeons that they trust to critically analyze their instruments and implants and provide feedback. This often involves a consulting relationship. The design of implants and instruments must be done with the surgeon in mind. Although there are many brilliant biomedical engineers, unless they have a thorough understanding of surgical approaches and possibilities, many concepts meet with failure. Bringing a design from paper into the operating room and making it effective require the involvement of innovative surgeons. In addition, once an implant or instrument design is created, other surgeons must be educated in its use. This training is best performed by surgeons with the support of implant companies. There is no other efficient way to transfer knowledge regarding new implants and techniques.

Assume for a moment that an extreme option was accepted. An extreme option would be that any individual who accepted money from industry for grants, consulting, royalties, or for travel would be unable to participate in research involving the products of those companies. It is my belief that this would have a chilling effect on innovation in orthopaedic surgery, particularly at university-based programs. Many university-based programs are currently dependent on industry-funded research.\textsuperscript{8} As the number of federally funded orthopaedic surgeon-researchers diminishes, industry-sponsored research projects have become the norm. Without such projects, the surgeon-researcher would be severely endangered. With the loss of this
money, much of the funding source for faculty and residents would be diminished. Currently, it is much easier for industry to sponsor clinical trials done in private-practice settings. Within a private-practice setting, a surgeon has less rigorous oversight from institutional review boards or university administration. It would be a shame if clinical trials were removed from the university setting and were performed only in private-practice settings. It is my feeling that this would drive many cutting-edge surgeons out of university programs so that they could participate in surgical innovation. In addition, university oversight is helpful to these clinical trials. It helps to keep a check on the industry and its enthusiasm for new product development.

The opposite extreme would also be unacceptable. Such an option would allow unlimited money from industry to individual surgeons without the need for disclosure, limitations, or management plans. This is severely damaging to our public perception and opens the door for direct financial profiteering from surgical decision-making. This gives the public the perception of “kickbacks” and of experimentation for profit. There is also a loss of investigator and university credibility, thereby imperiling the science of orthopaedic surgery. None of us will know what information to trust if the majority of our information is financially biased.

Clearly, there must be a more reasonable option. The middle ground, the sensible solution, should eliminate bias in surgical innovation. However, it should not eliminate progress in surgical decision-making. Not all conflicts of interest involve bias. It is the purpose of this manuscript to provide the sensible solution that manages conflicts of interest and allows progress to continue to be made at our university orthopaedic programs.

**Principles of Management**

First, we must identify the specific issue with which we are dealing. We must separate surgeon-industry conflict of interest from (1) poor medical ethics (medical entrepreneurship), (2) poor patient selection by individual surgeons, and (3) poor communications among surgeons, patients, and the media. Many of the issues outlined previously, and in the media, do not involve surgeon-industry conflict of interest. The decision that the surgeon must make about whether to perform an operation on a patient is a personal one, and it is totally reliant on that individual surgeon’s medical ethics. It has been and always will be our responsibility to maintain a high degree of medical ethics among our own practitioners of orthopaedic surgery. This begins with our education of medical students and residents and continues with our oversight of the orthopaedic surgery community. Unfortunately, these ethics have been eroded by a tendency toward entrepreneurship within orthopaedic surgery. High-profile, high-volume, highly marketed practices do not lend themselves to a high degree of medical ethics in decision-making. These for-profit practices do occasionally lead to poor patient results, as has been previously described in the media; however, they have nothing to do with industry-surgeon conflict of interest.

Particularly in spine surgery, poor surgical results have become high profile. The attempted class action status for pedicle-screw litigation and “cage rage” are both examples of poor patient selection. There is nothing inherently wrong with pedicle-screw fixation or with interbody cage fusions. However, when surgeons and patients alike use desperation and frustration as their two main surgical indications, bad results will predictably occur. It is often these frustrated patients who lend themselves to high-profile litigation and media sensation.

Poor communication with our patients and the media has also led to this misconception. There is no surgical procedure in orthopaedics that is 100% successful. Properly communicating complications and realistically presenting possible adverse outcomes to our patients preoperatively will severely curtail the disappointments in our patients postoperatively. Yet in many high-volume operative practices, this preoperative discussion is performed sparsely or by a subordinate. Poor results in these situations will lead to disgruntled patients and litigation. In addition, the orthopaedic community has been reluctant to go to the media to combat these individual stories. There are good data that show excellent results from well-controlled surgical trials of spinal fusion. However, these are often downplayed or ignored by sensationalist media who are looking to tell a specific story. The orthopaedic societies should be more proactive in showcasing good science that shows good results.

It is imperative as we craft a reasonable and sensible plan for management that we realize that the elimination of conflict of interest is impossible. Conflict of interest is everywhere. In practice, there is continual conflict between the needs of our hospitals, our insurance carriers, our training requirements for residents and students, the needs of our individual practice group, and that of patient interest. Although ethically we should always place patient interest first, these other needs always place us in some degree of conflict. Take, for instance, the specifics of cost containment. Hospitals are constantly applying pressure to have lower orthopaedic implant costs, shorter hospital stays, and lower use of radiographic studies. However, for each individual patient, we will often maximize care if we have our ideal implant of choice, a hospital stay that satisfies both the surgeon and the patient, and preoperative, intraoperative, and postoperative radiographic studies that show us the most exquisite detail. Balancing these two conflicts and obtaining good surgical results are part of our everyday practice. There is no way to eliminate these conflicts.

Within research, conflicts of interest are omnipresent as well. Even in pure basic-science research, the pressure to obtain repeat funding of a grant is immense. Those with federal funding need to obtain results in their grant that are positive to help to support their sec-
Principles of Managing Surgeon-Industry Conflict of Interest

The following are suggested as sensible principles in managing bias and conflict of interest (Table III).

1. Remove direct financial profit from the surgical implant decision-making process. I believe this is the most important principle in managing conflict of interest. The individual decision to perform surgery on a patient, and which implant to place in that patient, should not personally profit the surgeon. This means that the surgeon placing the implant should not receive any royalty for that implant, should have no increase in his or her consulting fee based on the placement of that implant, and should not have substantial (≥5%) ownership interest in the implant company.

2. All publications, whether health services, clinical, translational, or basic-science research, should include full disclosure of the author's conflict(s) of interest. Disclosures should be as specific as possible. Authors should disclose that they receive royalties, consulting money, research grant support, university-based support, or travel honorariums. This allows the reader to use his or her own judgment in evaluating the scientific conclusions reached in the paper.

3. Allow health services, basic-science, and translational research. When an orthopaedic surgeon does receive money from an industrial source for consulting, royalties, or in the form of research grants, this should not affect the production of basic-science and translational research. This research will be judged on its own merits in the peer-reviewed press and should stand as such.

4. Allow clinical research with appropriate management plans. The management plan should allow the surgeon to continue to participate in the study design, patient entry, performance of surgery, data collection, data analysis, and data reporting. However, to participate in these without bias, specific oversight by institutional review boards and/or research compliance officials must be present. Absolute disclosure of the conflict of interest must be made to the individual's institutional review board. Clinical studies must be designed to minimize bias in surgical decision-making. Patient enrollment, including a thorough discussion of the risks and benefits of the devices and/or biologics under study, should be performed by an independent practitioner, such as a research nurse. Prior to enrollment in a study, the patient should have a second opinion addressing his or her suitability for the study by a surgeon independent of the investigatory surgeon. Patient outcomes data forms filled out by the patient and questionnaires answered by an independent nurse practitioner are ideal. Radiographic review should be performed off-site by independent analysis whenever possible. Data analysis must be performed by an independent third party.

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<tr>
<th>TABLE III Conflict Management Strategy for Investigators Performing Clinical Trials Involving Orthopaedic Devices-Biologics</th>
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<tr>
<td>1. Neither the surgeon nor the institution in which he or she practices should receive royalties or other remuneration from the manufacturer for devices implanted by that surgeon.</td>
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<tr>
<td>2. All publications should include full disclosure of the author's conflict(s) of interest.</td>
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<tr>
<td>3. For investigators with financial relationships with industry, specific management plans are required to allow them to participate in clinical research. The principles of the plan include:</td>
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<tr>
<td>A. Oversight by institutional review boards and/or institutional research compliance officials is necessary.</td>
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<td>B. Disclosure of financial relationships must be made to the institutional review board.</td>
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<tr>
<td>C. Once a potential research subject is identified by the surgeon, enrollment, including a complete discussion of the risks and benefits of the devices-biologics under study, should be done by an independent practitioner, such as a clinical research nurse.</td>
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<tr>
<td>D. Prior to enrollment in a study, the patient should have a second opinion addressing his or her suitability for the study by a surgeon independent of the investigating surgeon.</td>
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<tr>
<td>E. Outcomes forms should be filled out by patients, when appropriate, or by an independent individual, such as a clinical research nurse.</td>
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<td>F. When possible, radiographic review should be performed off-site by an independent investigator.</td>
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<tr>
<td>G. Data analysis must be performed by an independent third party.</td>
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<tr>
<td>4. Restrictions on data reporting by the funding agency are prohibited.</td>
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<tr>
<td>5. Research subjects are entitled to be informed of all financial conflicts of interest.</td>
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<tr>
<td>6. Academic institutions and hospitals must work in concert with the investigator to facilitate clinical research.</td>
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5. Allow no restrictions on the reporting of data. Researchers who have ties to industry should not accept any restrictions on their ability to report the results of their trials.44

6. Research subjects are entitled to view disclosures. Under an appropriate conflict-of-interest plan, any investigator who has substantial financial ties to an industrial sponsor must disclose those ties to the individual patients.

7. Remove university-based blocks to clinical research. A university consortium for institutional review boards is suggested. Thus, if a multicenter trial was proposed and it was approved by a university consortium, then multiple universities would have approval on the basis of this consortium. This would streamline and hopefully facilitate multicenter clinical trials. In addition, trials sponsored by the Food and Drug Administration should have a waiver from the institutional review boards of individual universities. Since, in general, the Food and Drug Administration is rigorous in mandating patient entry, data collection, determination of success, and blinding of results, these trials should be exempt from independent university institutional review boards.

Conclusion
Although the panelists who participated in this symposium have differing views about the optimal management of the relationship between orthopaedic surgeons and the orthopaedic industry, all agree that this is a pressing issue that needs to be addressed by our professional organizations and their leaders. Furthermore, all agree that policies developed from within our profession are likely to be superior to those imposed by external agencies where the perspective of the practicing orthopaedic surgeon may not be represented.

Both before and after the symposium, the attendees were polled about various aspects of the orthopaedic-surgeon-industry interaction. It is instructive to consider their responses as our organizations address this issue. At the completion of the symposium, 76% of the attendees believed that there should be a prohibition of marketing by physicians for drugs or devices in which they have a financial interest. Ninety-six percent believed that there should be full disclosure to patients in the private offices of all doctors with regard to any and all financial incentives for patient care or clinical research. The respondents were nearly evenly split concerning the adoption of a policy that would prohibit clinical research on a drug or device by an investigator who has a financial interest in the drug or device, reflecting the split in the views of the panelists. Sixty-nine percent of the respondents indicated that there should be no policy proscribing the selection of journal editors, officers of major professional organizations, and leaders of academic institutions who have financial conflicts of interest.

Financial conflicts of interest are an omnipresent reality for orthopaedic surgery practitioners. It is incumbent on the individual surgeon as well as the organizations that represent us to manage these conflicts in an honest and ethical fashion so that the best interests of our patients are our highest priority.

Joshua J. Jacobs, MD
Jorge O. Galante, MD, DMSc
Rush University Medical Center, 1725 West Harrison Street, Suite 1063, Chicago, IL 60612. E-mail address for J.J. Jacobs: Joshua.jacobs@rushortho.com

Sohail K. Mirza, MD, MPH
Department of Orthopaedics and Sports Medicine, and Department of Neurological Surgery, University of Washington, Harborview Medical Center, Box 359798, 325 Ninth Avenue, Seattle, WA 98104. E-mail address: mirza@uwashington.edu

Thomas A. Zdeblick, MD
Department of Orthopaedics and Rehabilitation, University of Wisconsin, 600 Highland Avenue, KI/739, Madison, WI 53792

The authors did not receive grants or outside funding in support of their research for or preparation of this manuscript. One or more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Wright Medical, Zimmer, Medtronic, and Synthes). In addition, a commercial entity (Zimmer, Wright Medical, Medtronic, and Synthes) paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated. One author (S.K.M.) receives royalty payments from the University of Washington Office of Technology Transfer for surgical drills licensed by Synthes. The University of Washington Department of Orthopaedics and Sports Medicine receives endowment income from chairs funded by Synthes, DePuy, and Surgical Dynamics (a former spinal implant manufacturer). The author also conducts research from some of these funds and holds the Surgical Dynamics Chair for Spinal Research.

doi:10.2106/JBJS.E.01049

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