11 An Industry Perspective on Conflict of Interest

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David Korn, senior vice president of the Division of Biomedical and Health Sciences Research at the Association of American Medical Colleges (AAMC), said that "conflicts of interest are ubiquitous and inevitable in academic life, indeed in all professional life. The challenge for academic medicine is not to eradicate them, which is fanciful and also would be inimical to public policy goals, but to recognize and manage them sensibly and effectively."[1]

Who has to deal with conflict of interest? The answer is that everyone does. Therefore, the question is not who has conflicts of interest but whether conflicts of interest influence the results in science. (I will use the word "science" to include all of medicine and science.)

Conflict of Interest and Bias

It is critical to understand that having a conflict of interest does not mean that a person is biased. Conflict of interest does not necessarily lead to bias (but, of course, it can). The more important question is, if a person has biases, are they influencing his or her research design or research conduct? A researcher can be very biased in terms of opinions and beliefs and still do meaningful and unbiased research. When I worked full-time in academia, I knew many "professors" who clearly were biased in favor of their own pet theories and hypotheses. Yet they had a great deal of personal integrity and would not allow their biases to influence the research studies they designed

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or conducted. They demonstrated this phenomenon many times and some of them even won Nobel Prizes. The presence of investigator bias therefore does not necessarily mean a study or trial is flawed. The bias may *not* have influenced the results. Many biased investigators are objective and honest about their research and its interpretations. Both biased and non-biased investigators may have complete integrity.

Even if one's biases do not influence one's own research design or conduct, they still could result in biased interpretations of the data. Of course, if one's biases do influence research design or conduct, they almost invariably will lead to biased data or conclusions. It is quite common in science for people to have strong biases in favor of one theory or another.

We should not have a public goal of eliminating conflict of interest. The answer to the issue of conflicts of interest is not to seek to eradicate all conflicts of interest but to eliminate biases from influencing research results. This is done by peer review of manuscripts and other techniques.

Nonfinancial Issues

The media and the public generally focus on only financial conflicts of interest, and ignore other types. However, nonfinancial biases are often much stronger than financial conflicts of interest and often influence research results to a greater degree. One example of a nonfinancial conflict of interest is academic advancement, which I would add, also involves many issues of financial consequences. Winning grants and achieving tenure are obvious examples. Any increase in prestige and fame can also bring financial reward. A researcher with increased recognition can expand his or her research in many different ways. And increasing the number of people on the research team and/or extending the scope of the work itself can often lead to more grants being obtained.

Institutional Conflicts

Institutions may also have conflicts of interest. Institutions are like organic enterprises, almost like "beings." They, too, desire fame and glory and more research grants. Journals and popular magazines report grants like a baseball box score, showing which universities are going up and which are going down. They report the level of monies received from the National Institutes of Health, the number and type of stock shares they own, and various other categories. I am not questioning these practices, but they are evidence that institutions also have conflicts of interest, along with the biases that may result from them.

The desire of institutions to attract top scientists and students is strong and often spills over to the front pages of our nation's newspapers. Recently we read about Henry Louis Gates, Jr., and other people who are being wooed by one university or another. Universities also want important publications to come from their institution. They want royalties from licenses they have given to their patents. They also want their stock portfolio to rise (which is an important part of their endowment).

Managing Conflicts of Interest

Conflicts of interest are almost always managed effectively by researchers, companies, and the funding agencies through a system of checks and balances at multiple levels of oversight. This is the main reason why industry believes that the few true examples you hear about are rare occurrences and do not represent the "tip of the iceberg."

Industry adheres to rules on financial disclosure established by government agencies, such as the Food and Drug Administration (FDA). We have no problems with these regulations, and we have no problems with providing full disclosure. It is a prevalent myth that pharmaceutical companies pressure investigators to give them good data. The truth is that companies must have accurate data. Imagine yourself as head of a company or head of research and development. Your company has more drugs competing in the discovery phase

than you can take into clinical trials. You have more drugs in clinical trials than you can take to the market. You also have many drugs that are going to fail. How should you address this issue? The answer is that you want to get to the "negative answer" on a drug as soon as possible, and you design your trials to get to that negative answer. You do not figure out how to get falsely positive data, nor do you want false data. You want the most accurate information possible about the total clinical profile. Why? So you can put your resources on the breakthrough drugs and on those that are going to make money for your company.

Biased data not only could lead to developing a drug that may never receive FDA approval, but also, if approved, could lead to unnecessary product liability risks. Companies seek to do everything possible to avoid risk. The safest approach for a company is not to put new drugs on the market, but to be ultraconservative about those they do propose.

A few of the safeguards against bias influencing clinical trials include FDA rules on financial disclosure, FDA review of clinical trial protocols and informed consent forms, and Institutional Review Board (IRB) reviews of these protocols and forms. Many organizations have been working diligently to increase IRB standards, both through voluntary accreditation and through the use of Central IRBs. This latter concept is an important method that will decrease the workload of local IRBs, so that the government, academia, and industry, which may have a hundred or more sites in a clinical trial, have to go to only to a single Central IRB for the protocol's review.

Other safeguards include having the protocol reviewed by the clinical research unit where the trial will take place as well as by the institution's department. The trial design itself is often not just double-blind, but is triple-blind. Trials have statisticians who monitor the trial, sponsors who review the audits, watchdogs who monitor investigator integrity, and peer review prior to publishing. These constitute a large number of fail-safe systems to insure ethical behavior.

Pharmaceutical Research and Manufacturers of America

The Pharmaceutical Research and Manufacturers of America (PhRMA), which is the research industry's trade association, supports the efforts of the American Association of Medical Colleges and the Association of American Universities to assess conflict-of-interest issues. The American Medical Association (AMA) and PhRMA have formed a working group to inform physicians and sales representatives about the AMA's guidelines for gifts to physicians from industry. (These guidelines are now on the AMA's Web site). These guidelines should be considered for inclusion in conflict-of-interest policies of institutions.

Conclusion

The goal, from industry's perspective, is to have robust mechanisms and systems to minimize any undue influence of bias on research or its results. These mechanisms include institutional policies, monitoring, audits, regulatory reviews, and regulations on disclosure about potential conflicts of interest. The single most important message is that all of these mechanisms are in industry's interest, even though, from time to time, we may hear about problems that have occurred either there or in academia.

Endnote

1. David Korn. "Conflicts of Interest in Biomedical Research," *JAMA* 284, p. 2234, November 1, 2000.