# ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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## Conflict of Interest in Industry-sponsored Drug Development

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**H&O** How do you define conflict of interest?

**EE** Researchers have three primary interests: conducting scientifically valid research, disseminating the findings of research, and protecting the participants in research. However, researchers also have many other interests because we are multidimensional people. Professionally, we have responsibilities to our professional societies, to be good department members, and to positively mentor students and fellows. Additionally, we have responsibilities to our family and friends. Finally, we have our own goals of receiving recognition for our contributions to science. A conflict of interest (COI) occurs when a secondary interest undermines the objective and rigorous pursuit of good conduct in research, dissemination of results, or protection of participants in research. The worry is that money from industry might distort these three primary objectives and researchers' pursuit of them.

**H&O** How might industry sponsorship distort the process of conducting research in accordance with these goals?

**EE** Fairly strong data exist to show that industry-sponsored research, at least as designed, is as scientifically rigorous as, if not more scientifically rigorous than, research sponsored by nonprofit organizations or government. Industry-sponsored research is more likely to use double-blind protocols and randomization, more likely to preset the study endpoints, and more likely to describe adverse events in the literature. One explanation for this rigor is simply that the pharmaceutical industry often has hundreds of millions of dollars at stake, so the risk of failures in scientific rigor is associated with a hefty financial penalty. Furthermore, the industry is under constant monitoring by regulatory agencies, such as the US Food and Drug Administration (FDA), to ensure that studies are conducted in a rigorous fashion.

The second issue is the protection of patients who participate in the studies. There are no data—though a few anecdotes do exist—to suggest that people who participate in industry-sponsored studies are at greater risk. There are many reasons not to assume patients on such studies are at increased risk, and data have not yet been collected to suggest otherwise.

The third issue is the interpretation of data from trials. One well-done study by Stelfox and colleagues published in the *New England Journal of Medicine* in 1998 suggested that financial interests, whether in the form of research support, stock ownership, or other financial connections to industry, affect how scientists interpret data. Researchers who have industry-sponsored financial interests are more likely to interpret data in a way that is favorable to industry.

Finally, there is the dissemination of data. This is the area where the most disturbing data exist. The data indicate that industry-sponsored research is not likely to be widely disseminated when it is negative and is likely to be widely disseminated when it is positive. Industry does want to generate the data and conduct the trials in a rigorous fashion, but when the results are negative, dissemination of the data falters. It is understandable that industry has a great interest in generating sales of their products, and negative studies can negatively affect sales. Nevertheless, this is an area of great concern.

**H&O** What efforts have been made to improve the dissemination of data?

**EE** There have not been efforts by government agencies to improve the dissemination of data. In fact, though I

believe this issue needs to be addressed further, much of the data submitted to the FDA cannot legally be released to the public. It is my view that a better system of registering clinical research trials is needed in order to much more reliably ensure that all studies that occur do in fact have their data disseminated. A voluntary registration process is now in effect, mostly enforced by medical journals. This process is flawed because not all the important elements are reported, such as the primary endpoint being pursued. This registration needs to be generally enhanced.

**H&O** Could you describe how research has been conducted into COI?

**EE** The study by Stelfox and colleagues examined an area of controversy, the use of calcium channel blockers in hypertension, to show that researchers interpret data differently if they have a financial interest. The authors examined all the research reviews, letters, and other publications on the topic in major journals and then examined the financial connections of the authors of these articles. It was found that the articles that agreed with claims made by the industry regarding these agents were much more likely to be authored by those who had a financial tie to the industry. Other studies about the dissemination of data have looked at studies submitted to regulatory industries. Two well-known investigations of this type, particularly one by Whittington and coauthors published in *The Lancet* in 2004, relate to data on selective serotonin reuptake inhibitors. In these investigations, it was shown that the data submitted to regulatory agencies in Sweden and the United Kingdom included, in each case, many more negative studies than were published in the world literature.

Similarly, Eliot Spitzer, when he was Attorney General of New York, obtained e-mails from GlaxoSmithKline about one of its drugs, which argued that if negative findings were released publicly, the financial interests of the company would be negatively affected. This case led to some of the voluntary programs of dissemination of pharmaceutical trials underway. There is also evidence of other individual cases when industry has attempted to muzzle individual investigators; two famous cases of this type were at the University of California at San Francisco involving Boots Pharmaceuticals and at the University of Toronto, Canada, involving Apotex.

**H&O** Regarding disclosure of COI, what improvements have been made in recent years and what remains to be done?

**EE** There are several types of disclosure of COI. Disclosure to colleagues when speaking differs from disclosure to editors, and therefore to readers, which differs in turn from disclosure to research participants. There is widespread agreement that the first two types of disclosure are unassailable. Disclosure to research participants has been more controversial. Though many think such disclosure represents and important safeguard, data have been developed suggesting that is unlikely to be true. Research participants were asked if they were worried about COI and whether they wanted researchers' financial interests disclosed to them or if disclosure would change their decision to enroll in a research trial. It was found that participants were not worried about COI and, among cancer patients, disclosure of financial information would, in general, not have affected their decision to enroll. Many patients believed financial links were permissible. Our conclusion was that release of COI information to research participants would not constitute a strong safeguard if it would not affect patients' behavior as a result. At some remove, these data make a lot of sense—very sick patients are most concerned with receiving the best treatment, not with disclosure of COI. Patients assume that some system of oversight exists to ensure that financial COI does not compromise the research. Therefore, I believe it is important for institutions to put a system of oversight into place and tell research participants about its existence to reassure them that financial interests will not distort or compromise the study in which they are participating.

**H&O** Could you describe the effectiveness of institutional oversight?

**EE** It is unclear if the current system is effective. Researchers are supposed to disclose to their institutions what financial arrangements they have, and institutions are supposed to ensure the researchers are not involved in research studies with which they have a financial COI. If they do participate in such studies as researchers, a mechanism should exist to ensure that the COI does not distort the design, interpretation, or dissemination of the study. Rules vary from institution to institution, and many researchers do not know what the rules are. Good data on compliance with the rules do not exist. We do not have much assurance that policies on disclosure are being implemented effectively.

**H&O** How can it be assured that such policies are implemented in a more equal fashion across institutions?

**EE** An effort to implement one uniform policy applicable to all institutions is the starting point. It is difficult to understand why one set of financial interests are impermissible in California but not impermissible in Virginia, Maryland, or Illinois. Second, a much more robust

disclosure process is needed but it should not overly burden researchers. In the current system, researchers must disclose to every journal in which they publish, every time they speak publicly, and so on. This process is burdensome and inefficient. Finally, it is necessary to ensure that institutional review boards are attuned to the financial interests researchers have. Currently, we know that it is often the case that institutional review boards do not actually possess the complete set of data on financial interests related to the protocols they are charged with reviewing.

**H&O** Does the American Society of Clinical Oncology's COI policy work toward improving the disparity between institutions?

**EE** Hopefully the COI policy developed by the American Society of Clinical Oncology has a positive effect in terms of decreasing disparities because all oncologists are subject to the same standard. However, this policy increases complexity. I was involved in the development of the policy, and I do worry that the policy can increase the burden of disclosure. The system still has room for improvement in terms of efficiency. On the other hand, it has been useful in creating uniformity where it never existed before.

## Suggested Readings


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