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Innovation and industry-academia interactions: Where conflicts arise and measures to avoid them

■ ABSTRACT

Every phase of the development of biopharmaceuticals and medical devices has the potential for conflict of interest, but adherence to established rules and practices throughout product development can eliminate the possibility of conflicts. Adherence to good practices should continue through the postmarketing period, with swift reporting and vigorous investigation of any safety concerns. Although some academic medical centers are restricting interactions between their faculty and industry to prevent possible conflicts in physician education about new products, industry and academia should look for new ways to come together in mutually agreed forums that focus on educating clinicians about new products in an efficient, transparent way.

I have worked in academia and the pharmaceutical industry for more than 40 years. The potential for conflicts of interest between the two groups has always existed, but heightened recent concern has brought us to this meeting today.

Interactions between universities and the biopharmaceutical and medical device industries are important for two reasons:

- They are necessary to the discovery and development of new drugs, vaccines, and medical devices
- They are critical for providing scientific and educational information about new products to physicians for use in patient care.

I will review briefly the industry-academia interactions at each stage of the product development process in a key area of biomedical innovation—pharmaceutical development—with a focus on where conflicts can arise and how they can be averted.

■ DRUG DISCOVERY

Drug discovery generally takes place in industry but is

dependent on knowledge generated at universities. Certain basic research discoveries from universities are patented, as are all drug candidates discovered at universities. University patents can be licensed to an existing company or may be used to start a small company.

A number of financial interactions between industry and academia can occur at this stage, each of which benefits both sides and helps to build the biomedical enterprise in the United States. These financial interactions may include grants or contracts awarded to faculty who work on specific projects of interest to a given company, fees to faculty who are expert in a specific scientific area to consult with company scientists, or industry support of the training of graduate students involved in a specific project. Potential areas for conflict of interest exist since valuable confidential information is generated, but all universities and academic medical centers have rules in place for handling such information.

■ CLINICAL TESTING

Once a product candidate is identified by industry, it enters the development process. At this stage as well there is a need for university faculty—in this case clinical specialists at academic medical centers—to be involved in formulating a plan to take the drug candidate through all three phases of clinical trials. Faculty consult with industry physicians to design the clinical trials, act as lead investigators in clinical investigations, participate in data reviews, and help formulate a strategy for US Food and Drug Administration (FDA) review of the data.

These interactions—university experts acting as consultants to industry—are crucial to the innovation process. These faculty services are valuable to industry, and faculty are paid commensurate consulting fees for these services. At the same time, any inside information that is available to consultants must not be used in the trading of company stock.

The safety and welfare of human subjects can never be compromised by financial interests. Unless there are compelling circumstances to argue other-

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wise, a financially interested person may not conduct research on human subjects.

■ MARKETING OF NEW PRODUCTS

Once a product is approved by the FDA, it is ready for introduction to physicians. This involves the transfer of important information about the drug to prescribing physicians and to members of the formulary committees that control the purchase of drugs.

Getting this information to doctors requires publication of the clinical studies, presentations at organized medical and scientific meetings, and advertisements in journals, and it is heavily dependent on company sales representatives. These sales reps are highly trained to teach doctors and formulary committee members about the positive and negative aspects of a drug. They must discuss only the indications that have been approved by the FDA and they are trained to deliver a balanced discussion, covering the positive and negative features of a drug so that it is used safely and effectively. The trick is to get enough time in the schedule of a busy physician to deliver this information well. Since physicians have limited time and many sales reps are competing for this time, physicians must prioritize such visits.

An exciting new drug gives an advantage to a sales rep in gaining access to physicians, but such drugs are not available on a regular basis. To gain physicians' attention, the pharmaceutical industry has offered inducements such as free meals, modest gifts (< \$100 in value), free drug samples, and financial support of educational activities, such as continuing medical education and medical conferences.

New policies to limit conflict in education— and an alternate model

Yale University, the University of Pennsylvania, and Stanford University have recently prohibited certain interactions between their medical school faculty and industry to prevent possible conflicts of interest surrounding physician education about biomedical products. (See previous article by Stanford's Philip A. Pizzo.)

An alternate approach would bring together the two sides to develop more efficient ways for industry to educate physicians and formulary committees about products, such as scheduled on-site meetings during which company products could be discussed. In return for such access to groups of physicians, a company could support continuing medical education, offer travel grants for stu-

dents, house staff, and faculty, or support academic conferences. Transparency would be crucial to such a model.

■ POSTMARKETING SURVEILLANCE AND DRUG SAFETY

When given at high enough doses, all drugs have side effects, some of them serious.

During the large clinical trials required for FDA approval, patients who do not have certain comorbidities that might confound study interpretation are selected for inclusion. The number of patients in the trials and the study durations are limited based on prior agreement with the FDA. Adverse events that are identified during these trials are included in the drug's package insert that is approved by the FDA.

Of course, after the drug has been on the market with broader patient exposure, new side effects, some potentially serious, may surface. These are required to be reported to the company that markets the drug and to the FDA.

Recent years have revealed several cases of serious drug side effects that did not surface until this postmarketing surveillance period. Among the most prominent cases:

- The fenfluramine/phentermine combination, used for the treatment of obesity, was found to cause heart problems
- Certain antidepressants were found to increase thoughts of suicide in some children
- Cyclo-oxygenase-2 inhibitors were found to increase cardiovascular risks.

When an early signal of a possible adverse event is reported, the right thing to do is to determine as soon as possible if the event is caused by the drug and, if so, report the event to the FDA and carry out a vigorous investigation to characterize the side effect. If it is not serious enough to cause withdrawal of the drug from the market, then manufacturers should work with the FDA to explain the adverse reaction in the package insert and carry out a broad communication to all prescribers and patients so that the drug can be used properly with a full understanding of the risks.

As the cases above illustrate, early action is imperative. The most important charge that a manufacturer of biomedical products has is to represent the benefits and risks of its products accurately. Any mistake can destroy a company in addition to destroying patient lives.

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We need more efficient ways for industry to educate physicians, such as scheduled on-site meetings; in return, companies could support CME, travel grants, or conferences.