

The Role of Pharmaceutical Companies in Sponsored Research

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Pharmaceutical companies have relatively large research and development (R&D) programs. The top United States-based pharmaceutical firms had \$244 billion in revenue in 2006.¹ Assuming an average of 15% of revenue spent on R&D for companies developing new pharmaceutical treatments (<http://www.phrma.org>), this is \$36 billion in R&D expenses per annum. By comparison, the National Institutes of Health budget for fiscal year 2007 is approximately \$29 billion (<http://www.nih.gov>). Although portions of the research conducted by pharmaceutical firms occur intramurally, there is a substantial amount of extramural sponsored R&D—that is, sponsored research. This sponsored research has a potential impact on us in many ways—we may be the researchers contracting with the firms, prescribers of medications approved based on this research, or readers of publications forthcoming from this research.

Pharmaceutical firms' sponsorship of this large amount of R&D is related to their business goal of providing financial return for stockholders. The average usable patent life on a pharmaceutical is about 10 years. Thus, there is an ongoing need to discover and develop new pharmaceutical agents. Investment in a potential new product must be viewed from a financial perspective; time is money. The end goal of R&D is to gain regulatory approval for this new product, which will, in turn, generate product revenue for the firm.

In general, basic research aimed at determining how the body works tends to be conducted at academic institutions. This is because of the mission of the educational institutions, interest and goals of the researcher (faculty), and funding sources (typically government grants). Directed research (e.g., how receptors or enzymes function as drug targets, molecular modeling, synthesis of new chemical entities that target these receptors or enzymes) tends to be conducted at pharmaceutical firms—again primarily because of the researcher's interest, institutional goals, and funding sources.

Clinical studies as conducted by pharmaceutical firms are universally conducted under good clinical practices using clinical trial materials made under current good manufacturing practices. Nearly all clinical trials are conducted extramurally. Early-stage trials (e.g., phase I) are designed to evaluate primarily safety and pharmacokinetics in health volunteers. There is also a growing effort to obtain some measure of drug action (pharmacodynamics) in these normal volunteers by determining biomarkers for the drug target(s). Later-stage trials (e.g., phase II, phase III) also evaluate safety but are primarily intended to determine efficacy. During these trials, an assessment is made of the magnitude of the drug's effect and the optimal dose and regimen. Information gathered in early efficacy trials is used to select both the primary efficacy outcome measure and the sample size required for the pivotal efficacy and safety

studies. These studies are typically conducted at a minimum of 80% power for the primary efficacy outcome measure. In the U.S., since Congress passed the Kefauver–Harris amendment to the Food and Drug Act in 1962, pharmaceutical firms are required to “provide substantive evidence of safety and efficacy in well-controlled studies. . . .” This has been interpreted by the Food and Drug Administration to mean that at least 2 replicative studies must be conducted. The duration of the trial is consistent with the indication and patient population. For example, ocular hypotensive drugs for glaucoma are studied for a minimum of 3 months for ocular hypotensive efficacy and 1 year for ocular and systemic safety.^{2–4}

Extramural clinical studies sponsored by the National Eye Institute include large multicenter trials. The primary objective of these trials typically is to answer major public health issues such as treatment versus no treatment or surgery versus medical therapy. A single study with a minimum of 90% power is typically conducted. By their nature, such trials are usually of long-term duration— ≥ 5 years of participation.^{5,6} There are examples of the National Eye Institute and a pharmaceutical firm collaborating—for example, the Sorbinil Retinopathy trial⁷ and the SCORE (Standard Care vs. Corticosteroid for Retinal Vein Occlusion) study.

Marketing support studies are funded by and driven by marketing/sales functions rather than R&D. Thus, such support is typically aimed at current or soon to be launched products and may have goals different from those of the R&D groups.

Most quality journals and societies require a statement of the source of financial support and disclosure of potential financial conflicts of interest. For those with financial interest, these disclosure statements are relatively straightforward. The financial relationship with the manufacturer of the product under investigation can be none, contractual or consultative, or proprietary (e.g., stock or patent ownership). As well, the author may have one or more of these relationships with a competing firm.⁸

I have been an employee or consultant to pharmaceutical firms for 28 years. Thus, I am quite accustomed to disclosing my potential financial conflicts of interests when I present my research in meetings or in print. However, close relatives of mine, perhaps with different surnames, may also have financial interests that are not fully disclosed or apparent. I may have additional potential conflicts, not readily apparent and not financial in nature, that may influence my interpretation of science. For example, my higher education was at various campuses of the University of California. As well, my major avocation is cycling. Thus, I may view research from researchers who are University of California cyclists to be of higher value than that of others. While I was a University of California Regent and Chair of the Committee on Audit, the Univer-

sity of California adopted a statement of ethical values that addresses some of these concerns.⁹ When we listen to a presentation or read a journal article, we look to the financial disclosure of the authors. A financial relationship does not preclude good science—it just allows us to consider the source. As noted above, potential conflict of interest also extends beyond simply financial relationships. For example, a researcher may have spent much of his or her career determining the role of a particular receptor in a disease process. As a result, the researcher has a potential conflict in reporting research on that receptor—he or she would be more likely to interpret data as supportive of his or her hypothesis and less likely as contradictory.

It is my supposition that everyone has potential biases that could be financially based (e.g., I own stock in the manufacturer, my career [continued funding, promotion, tenure, etc.] depends upon obtaining publishable results) or intellectually based (e.g., “my” enzyme is important to this disease and its treatment). Ideally, this should be disclosed and every effort made to minimize the potential of bias—for example, by appropriate clinical study design.

In summary, pharmaceutical companies are best for some types of research (e.g., new drugs/products; research resulting in regulatory agency approvals; research compliance [good laboratory practices, good clinical practices, current good manufacturing practices]), and academic and government institutions are best for other types of research (e.g., basic research, big-picture public health issues [drugs vs. surgery⁵], off-patent drugs [e.g., 5-fluorouracil¹⁰], novel uses for existing products).¹¹ Pharmaceutical firms have an important role to play in sponsoring research. The fact that these firms are for profit visibly raises the issue of conflict of interest. However, conflict of interest is an issue for all research, even that sponsored by independent institutions such as academia or government research centers. However, conflicts of interest do not necessarily invalidate research findings. Rather, these potential conflicts need to be disclosed, and a fair balance attempted.

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