



Conflicts of Interest in the Development of Animal Drugs

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The past 25 years have witnessed remarkable changes in how new drugs are brought to the market. Pharmaceutical companies once took pride in vertical integration. Animal tests, laboratory analyses, and clinical trials were conducted in-house. Even when companies found that many of these services could be done more effectively by contract research organizations, they maintained tight control of their research programs. Academic scientists frequently reported stories about efforts to contact a pharmaceutical company with an idea about a new drug only to be told politely that if the idea were not developed in house, big pharma was not interested.

Universities had their own ideas about the role of academic scientist in commercial drug development. When I joined the Johns Hopkins Medical School faculty in 1972, I was given advice by the Dean. "Academic research is a privilege. Get grants. Publish reports." If I wanted to become involved in the translation of my research, I would be told, "Good luck and good bye." This was conventional advice in academic centers. Although there were solid examples for successful partnerships between academia and drug companies, for example the Nobel Prize winning development of streptomycin for the treatment of tuberculosis [1], there were numerous stories about academic scientists finding negative results about a promising drug and being threatened with law suits by industry not to publish the findings. Journal editors avoided manuscripts, including reviews from scientists who had received money from industry [2]. There were concerns that scientists who took money from industry "owed" the drug companies. Conflict of interest (COI) policies at many leading journals effectively became one more tool to inhibit academic drug development efforts.

Today, industry-academic drug discovery consortiums are common [3]. At my university, the Office of Technology Licensing holds frequent meetings with research leaders of major drug companies to discuss potential for collaboration. Deans at one time promoted their universities based on the number of faculty who were in the National Academies, edited journals, and wrote key text books. Licensing income from technology innovation now can be added to that list. For the year 2011, industries reported \$1.8 billion in earnings from commercializing academic research. In addition, responding to a survey of the Association of University Technology Managers, 157 universities reported they had completed 5,398 licenses and filed for 12,090 new patents. They also created 617 start-up companies [4]. A recent letter from the Dean to our faculty said, "One thing we have not been known for, historically, is our entrepreneurial activity. There, we lag behind some of our peers, like Stanford and MIT, where new startups seem to sprout daily. But we've been steadily changing that by taking steps to strengthen our innovation ecosystem. We are working to foster an environment where people are encouraged and supported to translate their discoveries into real-world applications that have tangible benefit for patients [5]."

Academic Challenges

If ideas about academic-industry partnerships have changed in the

Dean's office, they have been slower to change in faculty lunch rooms. Investigator-initiated research proposals have been a corner stone of science in the US. For decades, investigators could briefly describe how their ideas potentially could lead to new drugs in the "significance" section of their grant applications. However, academic scientists are cautious about the new emphasis by federal and non-governmental agencies on examining this section from a business perspective. Few academics have acquired the skill sets or partnerships to translate research into the therapeutic marketplace. Second, faculty may well wonder if commercial activity that does not lead to block buster drugs will affect crucial promotion decisions. Will research supported by industry funding be ranked lower than grants from the NIH or private charities? Yet another concern is publication of industry-supported research. Will this support be flagged by journal editors? Reports of un-reviewed manuscripts listing industry sponsorship are common.

These concerns are magnified for scientists interested in veterinary drug development. There has been a 12 year slide in biomedical funding. Funding for animal drug research from government and non-profit agencies is a small percentage of the money available for the development of human drugs [6]. Recent shifts in federal priorities have placed even more translation emphasis on the limited funding. Small Business Innovative Research, The National Center for Translational Sciences (NCATS) of the NIH, and many state biotechnology grant proposals require specific information about how the research will be commercialized. In Maryland, for example, biotechnology grant applications go through both business and science review sections. Looking forward, the proposed 21st Century Cures Act, which has moved through Congress with strong bipartisan support, over the next ten years provides 10 billion dollars in biomedical funding for research emphasizing patient cures.

Conflict of Interest and Bias: Opinions and Evidence

Studies have shown that gifts from the pharmaceutical industry likely influence prescribing practices by physicians [7]. This type of evidence coupled with intuitive assumptions that commercial activities increase the risk of bias has primed the anti-industry concerns at many levels. Books with provocative titles such as *Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients*, and *The Truth About the Drug Companies: How They Deceive Us and What to Do About It*, hardly dampen the skepticism. Yet empirical evidence to support bias and COI is scarce. A study examining 76 US Food and Drug Administration (FDA) product approval votes showed that the voting outcomes would not have changed had all members with COI been removed from the voting panel [8]. In a recent series of reports examining COI associated with the pharmaceutical industry, Rosenbaum reports that intuitive assumptions that the greater the financial stakes involved the greater the risk, are not supported by evidence [9].

Conflict of Interest policies have been instituted by many professional societies and universities receiving industrial support. The

policies are based on transparency and depend on full disclosure of industry ties and financial interests. Critics may argue that university COI policies are primarily aimed at protecting the university rather than the reader of a report describing the safety and efficacy of this or that drug. But such an opinion rests on little evidence. Readers of published reports can make the determination whether the author's biases affect outcome reporting. In the development on new veterinary pharmaceutical products, the FDA has added additional protections. Sponsors of new drug applications are advised to fully review drug testing protocols with officers at the Center for Veterinary Medicine before starting safety trials. Sponsors cannot select tests that most likely emphasize safety and avoid those likely to expose problems.

Bias based on industry support is inherent in the design and reporting of any research. But undisclosed biases have been identified at many levels in academic research [10]. Whether fully disclosed industry support poses an unbearable COI at the faculty promotion committee or the door to the journal office is an ongoing question. A companion question is whether new and better animal drugs can be developed absent funding aimed at commercializing the product. Reasoned approaches to managing COI are being darkened by opinions rather than evidence [9]. Is a divide between academics and industry in the best interest of new drug development? Opinions are shifting among journal editors and leaders in research support. The President's Council of Advisors on Science and Technology, The Gates Foundation, The Wellcome Trust, the NIH and the FDA are among institutions encouraging greater interactions between academics and industry [11]. Can we move the conversation from one driven by suspicion toward one that better accounts for the diversity of interactions, the attendant trade-offs, and the role of industry in the development of new veterinary pharmaceutical products.

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