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Collaborative conflicts

Twenty years ago it was standard practice in the petroleum, chemical and pharmaceutical industries to discourage publication, particularly if patents were involved. However, biotech start-ups shunned the traditional industry approach to scholarly publishing. Founded by entrepreneurial academics, these companies were venture capital–based and understood publishing as a way to bring accolades to the company, which increased venture capital investments and stock prices.

Millions of dollars are now spent by the maturing biotech industry to produce and test drugs of interest. Partnerships are formed with universities and academic hospitals that allow access to patients and research expertise, which aid the design, implementation and evaluation of drug trials. If the results are positive, then the normal course of events is joint publication. But what if the results are negative?

About a year and a half ago a clinical trial run by the Immune Response Corporation (IRC) and their chief university collaborators, James Kahn from University of California at San Francisco (UCSF) and Stephen Lagakos from Harvard, was halted. Remune, an HIV "vaccine", had been evaluated in 2,527 HIV-infected volunteers for possible beneficial therapeutic effects. An independent group had reviewed the collected data and determined that there was no overall benefit to patients. The company and the chief academic investigators could then not agree on how to publish the results. IRC insisted on inclusion of a retrospectively reanalyzed subset of the data; viewed in this manner, IRC claimed that treatment perhaps had a beneficial aspect. However, the university investigators writing the paper disagreed with the methodology and would not include the analysis in their paper. The company then withheld the latest patient data (which included final patient visits and other crucial information), causing the authors to base their conclusions on a dataset that was only about 90% complete but similar to the dataset that led to the halting of the trial. IRC also refused to disclose the names of other researchers in the study, so not all investigators reviewed the paper before submission; subsequently some have expressed disagreement with the conclusions. Despite the company's objections, the academic scientists went ahead and published the paper (*J. Am. Med. Assoc.* **284**, 2193–202). IRC is now seeking damages from both UCSF and Kahn for over US$7 million for public disclosure of confidential data, a charge denied by the university scientists.

The Remune saga illustrates the complexities of industry-academic collaborations. The authorship issues generated by multicenter trials are compounded by sponsors seeking to exert control over a study's conclusions. Although biotech companies and academia both strive to improve public health, the ultimate goal of the biotech industry is to provide profit for shareholders. Along the way, new treatments, cures and palliatives are made available. The goal of university medical researchers to further our understanding of disease pathogenesis is combined with a need to gain stature through publication of reputable research. Publication of unfavorable results may be detrimental for a company but is in the interest of researchers and the public. Thus, clinical trials sponsored by a product's developer are often inherently conflicted. Yet industry funding is necessary, as public funding for clinical research is inadequate (in 1999 most of the National Institutes of Health US$17.8 billion budget went to basic research, whereas major pharmaceutical firms spent US$22.7 billion primarily on clinical research).

To manage the conflicts that inevitably arise, universities and biotech companies develop contracts that delegate responsibilities and enumerate expectations. Not all universities have solid conflict-of-interest policies, conflict-resolution mechanisms or guidelines that are regularly updated, but these are essential to deal properly with the reality of industry-academia collaboration. Increased public funding for clinical research would also remove some of the pressure and conflicts surrounding academic participants.

The Remune case is unusual in that issues were not resolved before publication. But negative data remains a problem. Studies indicate that unfavorable results concerning a sponsor's product are published less frequently and with greater delays. However, industry is not legally obligated to publish trials that fail. The limits of a sponsor's authority over data and interpretation require better and clearer definition. Suggestions of "data-spinning" undermine the company's reputation in the long run. Choosing which unfavorable results to release presents a challenge to both companies and academia. A researcher's right to view and publish results and the public's right to know are as important to protect as a company's investments. Only if appropriate safeguards for all parties are put in place will clinical research not be the ultimate victim.