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EDITORIAL

How Everybody Wins When Playing by the Rules: The Benefits of Investigator-Initiated Industry-Sponsored Clinical Trials

The medical device industry is a fast-growing field contributing many new treatment options for a variety of conditions every year. In the field of interventional neuroradiology, many devices are approved for use each year by the United States Food and Drug Administration (FDA) with little meaningful data.[1] While industry-sponsored trials for medical devices can help physicians further understand the safety and efficacy of medical devices, there is reason for concern regarding bias in the results of these trials.[2-4] Many studies have demonstrated that industry-sponsored clinical studies are significantly more likely to demonstrate positive results for industry-developed devices than their non-industry-sponsored counterparts.[2-4] Furthermore, there is much concern regarding real and potential abuses of physician-industry relationships. With so many approved devices on the market with little or no meaningful data, postmarket industry-sponsored research is essential in presenting more data to physicians and regulatory boards. However, the intrinsic qualms associated with industry-sponsored research provide a certain dilemma regarding improved postmarket surveillance.

How We Got Here

Medical devices in the United States are subject to significantly less regulation than pharmaceuticals. The FDA has "classes" of medical devices ranging from class I (with minimal potential harm, such as elastic bandages, surgical gloves, and so forth) to class III (which support or sustain human life; are of substantial importance in preventing impairment of human health; or which present a potential unreasonable risk for illness or injury; devices such as deep brain stimulators fall into this category).[5] Class III devices require the most rigorous scientific and regulatory review to assess their safety and efficacy. Most devices in interventional neuroradiology fall into Class II. Clearance for marketing of Class II devices means that the device must be "substantially equivalent" to previously ap

proved devices. However, large clinical studies are not necessary for proving substantial equivalence.[1,5] Furthermore, some devices can be approved with a humanitarian use exemption (HUE), which allows the device to be marketed as a humanitarian-use device. For a HUE, one must demonstrate that the device is safe and that there is "probable benefit" in a population affected with a disease or condition that is manifested in fewer than 4000 patients a year.[1] Despite approval with limited evidence, many payers are willing to pay for procedures with these devices.

As discussed previously, the physician-industry relationship provides an ethical dilemma because physicians are responsible for the needs of the patient while industry is responsible for the needs of the shareholder. Naturally, the medical device industry wants to find the most business-friendly path to marketing their device. By receiving approval of their devices through HUEs or through minimal evidence demonstrating "substantial equivalence," they limit their premarketing costs. Furthermore, in rapidly advancing fields such as interventional neuroradiology, physicians are in genuine need of new devices to treat new and difficult problems. The enthusiasm of using new devices coupled with aggressive marketing techniques makes it much easier for physicians to embrace these new technologies. Many physicians think these new technologies are in the best interest of their patients. With FDA approval and payer coverage of new medical devices, there is little incentive to pursue resource-intensive studies to evaluate real-world device performance. This is seen in 2 recent devices, the Neuroform (Boston Scientific, Natick, Massachusetts) and Enterprise stents (Cordis, Miami Lakes, Florida), which were used for years before any meaningful postmarket research was published.[6]

Possible Solutions

Collection of large amounts of postmarket data is essential to further the understanding of new devices by the medical community. Postmarket data can help in detecting serious adverse events associated with device deployment that may not have been present in smaller premarket studies. Long-term problems associated with implanted devices can also be detected in postmarket studies. Furthermore, large postmarket studies can help in detecting problems due to improper or unskilled use of new devices in a real-world setting because premarket studies are often performed by highly trained practitioners.

One possible means of encouraging industry and physicians to provide postmarket data demonstrating the efficacy and safety of a device is to require such evidence for payer coverage. This has proved to be effective in the case of carotid stents and the Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial funded by the National Institutes of Health (NIH). However, with the multitude of devices that are approved and marketed every year, it is impossible for nonbiased agencies such as the NIH to sponsor safety and efficacy studies for all new devices. One realistic solution to this funding dilemma is to have industry collaborate with physicians and pay for rigorous postmarket studies.

In arguing for physician-industry collaboration and industry-sponsored research, one must consider the practical and ethical implications. There are a number of benefits to industry-sponsored research, especially if it is performed in a cautious manner to avoid potential biases. Industry-sponsored research, if investigator-initiated, may well pass the "sniff test" of scientific validity. Many analyses have demonstrated that physician-initiated studies are significantly less likely to report results favorable to industry than industry-sponsored industry-initiated studies.[2-4] In investigator-initiated trials, the investigator acts as a sponsor-investigator. The individual investigator's role in these trials is to plan, design, conduct, monitor, manage data, prepare reports, and provide oversight for the study. The role of industry in physician-initiated industry-sponsored trials is limited to checking data for serious adverse events, notation errors, and omissions.

Trials initiated and funded by industry allow industry greater involvement in writing protocols, training investigators, and helping in data collection and analysis, thus potentially biasing data. Furthermore, it has been demonstrated that physician-initiated industry-sponsored research is associated with less overhead cost for the academic institution than industry-initiated industry-sponsored research.[7]

The investigator-initiated research model is well known in the medical community. As of 2006, 72% of pharmaceutical companies had active investigator-initiated protocols. These studies represent an effective means of collecting robust postmarket data that could benefit the medical community as a whole. In postmarket physician-initiated industry-sponsored trials, physicians are given an opportunity to use and develop an expertise in a new device. Patients enrolled in these studies will be afforded excellent long-term follow-up, given the importance of long-term data to such studies. Perhaps most important, medical industry, regulatory agencies, physicians, and patients will be given extensive data on the efficacy and safety of new devices, thus impacting future development, approval, payment, and the use of these devices.

There are a number of potential limitations to physician-initiated industry-sponsored research. First, this is a relationship that can be easily abused. Physicians may be given unethical incentives for providing good data; these incentives may include financial awards, material awards, or promise of future research funding. Physicians participating in industry-sponsored research, to avoid "biting the hand that feeds them," may feel obligated to provide favorable data to secure funding for future projects.[8,9] It would be hard to imagine a company continuing to fund a researcher who continuously demonstrates poor results with their medical devices. Thus, medical device companies may find investigators who have been known to publish "good" results on medical devices, thus increasing the bias of clinical data. Furthermore, physicians may be eager to enroll patients in these studies and may risk steering patients to receive treatments or devices that they may not necessarily need. These potential limitations must be addressed to establish a safe unbiased means of providing safety and efficacy data for newly approved medical devices.

The medical device industry is a $350 billion a year industry that is expected to grow at a rate of 10% annually in the near future.[10] The amount of funds available for device research from these companies far outstrips funding from governmental and nonprofit organizations. We, as academic physicians, must accept the reality that the medical device industry is playing and will continue to play an active role in the funding

of postmarket research of new medical devices. We think that the best means of limiting the potential biases of industry-sponsored research is to have this research be physician-initiated rather than industry-initiated. Furthermore, to reduce the bias associated with device companies funding proposals by investigators deemed "favorable" to the interests of industry, creating an independent organization that evaluates research and funding proposals for investigator-initiated studies would be beneficial. This would limit the role that industry plays in clinical trials to that of funding only. This sort of organization was proposed by the International Consortium of Neuroendovascular Centers (ICONE). ICONE is a group founded by a number of neurointerventionalists and dedicated to improving the field by providing funding and open access to data for research on new endovascular techniques and devices.[6]

This consortium seeks to partner with industry in this endeavor. Given the benefits of industry-sponsored research for the medical and patient communities, projects such as ICONE are certainly a step in the right direction. As clinician-scientists, we must continue to work to find ways to provide meaningful data while eliminating bias.

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