

Medical – Industry Relations

Chris Cates: I thought we had a tough job in interventional cardiology, but according to your presentation, it sounds like the device industry has it even tougher! Incentives within the system seem to be misaligned, and many cross-incentives exist, all of which causes a great deal of aggravation. If these incentives could be aligned appropriately, costs would be reduced throughout the system and quality of care would be improved as well. The HCFA bypass project proved that this could be done: the financial incentives were aligned with the technology and care incentives, costs were driven down and enormous advances were achieved in the quality of patient care and innovation. It's a shame that this model is not implemented more extensively. Reginald Low, who practices in California, an intensive HMO managed care model, could perhaps provide some insight on how a staff model HMO would be helpful in testing some of the aligned incentives between industry and cardiovascular care in which the provider benefits from cost-effective quality measures.

Reginald Low: Clearly, industry is a business; hospitals have become a business; and, to a large extent, medical practices have become a business. Industry, in my view, has done a much better job at conducting business than hospitals have. Medical practices fare well because medicine is fun; it's intellectually stimulating and rewarding — plus physicians get paid for it. However, physicians are now forced to focus more on the business aspects of their practice. While I think that industry is providing us in large part with what we need, it is always in their best interest to improve shareholder values by increasing earnings. Industry closely studies the marketplace in an attempt to fulfill our needs and thereby meet their objectives. What physicians and industry want is ultimately very similar, but the motivations behind these desires differ. Industry is motivated by money; physicians are motivated by patient care.

California, for example, is facing a very serious problem with the HMO system which has not been as successful as had been hoped. First of all, the HMO system has created a major problem in terms of medical manpower. It is virtually impossible to recruit subspecialists in California today because a physician can get paid twice as much elsewhere. Unless a subspecialist has specific ties to California, there is no incentive to work there. One positive contribution of the HMO system, however, is that it has taught practitioners how to better manage their resources and thus practice more cost-effective medicine without affecting long-term patient outcomes. Physicians are less likely to abuse the system by ordering an echocardiogram every six months, or an annual myocardial perfusion scan, because while these tests can be justified for a patient on a one-time basis, overuse of these tests would deplete the resources allocated for a specific subspecialty. Many of the practices across the country are now too focused on the business aspect of things. Physicians are trying to extract as much profit as possible and improve their own shareholder value. This trend will

be difficult to regulate and change — and I realize that this topic is not within the scope of this meeting's agenda. Despite its faults, managed care has actually taught us some valuable lessons which we should try to apply elsewhere.

Industry has been very good at providing new technology and supporting clinical trials. Greater value could be derived from these clinical trials if industry would support some additional areas of research within these very large clinical trials. Many advances in medical science could be achieved at very little additional cost to industry and would be of great benefit to patients and the medical profession. Industry has done a great job in terms of funding fellowships. Medtronic and Guidant, for instance, fund electrophysiology fellowships through NASPE. More of these fellowships are needed because, as you all know, the number of interventional fellows will probably be cut in half this coming year due to the new board and medical school affiliation requirements. Furthermore, a good deal of clinical work that has been funded by industry goes unpublished. This work is actually conducted by academic institutions and would, from a scientific perspective, be of great value. This research should be made available to the academic community because it would advance science at very little cost to industry.

Paul LaViolette: It is very frustrating to know that much of the pre-clinical work is done in order to be included in a 15,000 page PMA submission. The research then sits there for a long time and eventually receives approval. Can any of you think of a better way to expedite the FDA approval process without wasting valuable time and research or creating unnecessary data that most other countries don't even require?

Robert Falotico: I am not sure that that is the right way to go, Paul. The physicians who conduct research for Cordis have to appreciate the fact that industry drills many dry wells. We invest in areas that are not always fruitful. I would cite radiation as an example in which Cordis and other companies have invested very heavily. Some of the work has born fruit, but I am not confident that radiation will end up being quite the opportunity that was anticipated. A large amount of money has been invested in radiation and much has been learned, but drug-eluting stents represent a new area that involves therapeutics — and device companies are not as familiar with therapeutics. The drug-eluting stent is more of a pharmaceutical model in terms of development costs and requires the type of evidence and investment that is customary in the pharmaceutical industry: extensive and costly animal testing; drug licenses; new manufacturing operations; clinical trials, and so forth. In 2002, Cordis will be conducting approximately twenty clinical trials involving drug-eluting stents. The cost of bringing this product to market is very high. I have heard the number of \$100 million, but quite frankly, our numbers are considerably higher than that. Thus, it is important to recognize that this new technology is expensive and risky. Companies such as Cordis,

Boston Scientific, Guidant, and Cook are venturing out into uncharted waters. Industry is undertaking substantial risk and physicians are our partners in this process; you are conducting clinical trials with us, and we are learning together.

Chris Cates: But is this truly uncharted territory, or is it similar to 1993–1994 when Johnson & Johnson I.S. was producing the new stent with similar arguments? Ultimately, the stent launch became a Harvard Business School business model. Are we perhaps going to repeat that with pricing structures for drug-eluting stents?

Robert Falotico: I certainly hope not. What we are trying to provide is value and alternatives to surgery. The cost of new drugs is high. I think you have to look at the drug-eluting stent as a new way of packaging a drug. New therapeutics are expensive — that's the point I am trying to make here. Cordis and the other companies involved in this area are committed to delivering this new technology at the appropriate value and price.

Paul LaViolette: I am quite confident that the marketplace will take care of things. If the prices are too high, penetration will diminish, market value will not be generated, and companies will very rapidly reconsider their pricing strategies. We spend a considerable amount of time and money strategizing over what the initial price should be, and then spend all of one minute changing that price if it does not work. I am thus less concerned about that issue and am more focused on the 99% of other technologies, because I do agree that the drug-eluting stent business is considerably different and novel. Filter wires, carotid stents, and so forth, will be routinely used around the world and will simply not allow U.S. access.

Chris Cates: But initially, I.P. and regulatory barriers will allow a drug-eluting stent monopoly to exist for quite some time during which no competitive forces will act on the price of these stents.

Paul LaViolette: During the first year, at least three companies will be involved in the drug-eluting stent market. The stakes are so high that it is not at all unreasonable to think that one of those three companies could readily break rank in an effort to gain leading market share. Much depends on the data which are not yet available for all of the products, as well as how one product will be distinguished from another. Industry is in this for the long run. If there isn't a balanced value equation for the customer, then we don't care what the accountants say; they don't run the companies.

Kirk Garratt: You said something to me the other day during lunch, Bob, about the fundamental difference in the mindsets between device companies and drug companies with respect to return on investment, philosophies, and expectations. Would you comment on that for the group?

Robert Falotico: The pharmaceutical world is very research-intensive, whereas the device companies tend to develop products more rapidly. The cycle time in the device world is relatively short. It's difficult to imagine spending a significant amount of money to bring this new technology to market and not derive some benefit from it for a long period of time. I know there will be competition in the drug-eluting stent field. Competition is a good thing, and it will ultimately bring the prices down to a reasonable level.

Kirk Garratt: What I heard you say yesterday, Bob, is that drug companies and device companies have fundamentally different expectations about the return on investment. Perhaps it is underpinned by the fact that drug companies must spread money so much more broadly. For example, an antibiotic for a given disease may involve not just researching one or two possible drugs, but *fifty* possible drugs. Thus, the drug companies are required to pump money down many different channels simultaneously. Their expectation, therefore, is that when that one drug in fifty is found, a considerable profit margin must be realized in order to cover the initial investment and offer a reasonable return for the investors and stockholders. On the other hand, you talked about how the device companies are fundamentally different. No company has fifty atherectomy catheters under development at any given time. And even though the costs may be considerable to develop a single device — or two or three iterations of a device — the up-front expectations are that the incremental profit margin on each device, once marketed, maybe need not be quite as large as for a drug because this investment/payoff relationship is different in a fundamental sense. Am I reflecting your thoughts accurately?

Robert Falotico: Yes, absolutely. At the outset, I said that industry drills many wells and is fully committed to this new generation of therapeutic devices. We talked about entering the neurovascular arena as well. Vulnerable plaque is an area our company and others in the industry will be devoting time, money, and effort to. I am sure that a lot of what we do will end up on the “cutting room floor.” When a product this novel is brought to market, a higher profit margin is expected.

Paul LaViolette: I agree, but a company's bottom line is revenues — regardless of what business it is involved in. Two key factors are of concern: 1) the cost of goods, which leaves a gross margin; and 2) the percentage of sales devoted to research and development. The Profit and Loss for a drug company or a major cardiovascular company reveals that both of these companies are spending 12% to 14% of sales on research and development. Thus, it is less an issue of how many dry wells are drilled, but rather, how much money is needed for the drilling. As long as the research investment is not substantially greater than 10% to 15% of sales, then the basic financial model does not differ. As long as the gross margin on that product is 80%, I can guarantee you that a stent and a drug are not fundamentally different in terms of their profitability. The drug companies do have one advantage in that they may ultimately enjoy ten to fifteen years of viable protection for their new drug, whereas the stent will change much faster. Thus, in some regards, the device companies have a larger burden; they may reap a comparable financial reward on paper, but its duration is considerably shorter.

Gary Roubin: I enjoyed your discussion very much; you offered some excellent insights. However, you omitted one critical element: the relationship between industry and physicians. I am talking specifically about the physician who is a shareholder in the large or small company. The physician has considerable influence on the analysts and on Wallstreet — and the influences on Wallstreet are what affect the capital-raising markets. This incredibly important issue has been somewhat skirted here.

On another topic, requiring companies to provide twelve-month data on non-implantable embolic protection systems is ridiculous and represents another example of how we are unfairly and unreasonably over-regulated by the FDA.

Paul LaViolette: With regard to your comments about distal protection devices, the protocol actually requires 90-day follow-up — it's a 510K with clinicals. The good news about distal protection devices is that they fall under the Class II, not Class III, category. The actual clinical follow-up requirement for a distal protection device in the SVG trial, for instance, apart from the carotid system, is a much shorter time frame. Thus, the FDA does realize that the device is not an implant, but rather applies to an acute event as opposed to a long-term outcome event.

The conflict of interest issue is indeed interesting. I actually had prepared some thoughts on this topic originally, but its complexity would not allow me to adequately address it under this meeting's time constraints. I don't think that the entanglement is always healthy, but it is definitely a reality. Analysts call physicians whose comments can have massive impact on company value. Physicians understand the capital process and are very inventive and involved in device conceptualization which ultimately leads to ownership positions. I don't have a problem with that; it doesn't matter what the source of the idea is or the company's structure. The sole issue is: What if physician involvement becomes entangled with clinical results leading to a legitimate financial conflict of interest? Greater disclosure is needed. There is an increasing number of small companies with cardiology-based founders/investors; that is the nature of the game we're playing today.

Jeff Werner: What bothers me most about this entanglement is that those of us who work both as clinicians and administrators are faced with the conflict of a desire to deliver good patient care, on the one hand, and the increasing regulatory constraints on our practice, primarily in the form of Medicare and recent reimbursement decreases, on the other hand. Both hospitals and physicians are under increasingly stressful, and sometimes untenable situations. My hope is that we can reverse this trend.

Paul LaViolette: It is indeed a crucial issue. I was struck by a brief story that Tom Linnemeier shared with me regarding his role at Guidant where he brought a former administrator for HCFA, into the cath lab at Washington Hospital Center for two days. She observed two days of interventional procedures that went from balloon, to cutting balloon, to rotational atherectomy, to three stents, and so on. She was awestruck by the realities of the interventional process. She told Tom that she wished she had known this a couple of years earlier. Knowing HCFA, I'm not sure it would have mattered. The real issue is how to connect the dots throughout the entire budgeting process. Private and public

payors don't consider the total span of care. Government does not consider the cost-effectiveness of healthy people or that technology should be viewed as a money-saver over time instead of a short-term expense burden. These views represent amazingly short-sighted financial management in worldwide health care systems.

Chris Cates: The ACC has been very active in trying to push the process of global pricing strategy within interventional treatment. It is expanding the model for the HCFA bypass project, which is scheduled for implementation in the first quarter of 2002 in Ohio, Michigan, and one other midwestern state. The ACC will establish global pricing for the technical component, which is the hospital side, as well as the physician professional practice component for interventional treatment. This may at least align some of these incentives and tie them to cost and quality. The ACC initially called the project *Centers of Excellence* but changed the moniker so it didn't sound so exclusive. It's all about measuring quality indicators and rewarding physicians for achieving quality results over time — which is quite novel for a CMS to consider.

James Zidar: I have spent a good deal of time over the past couple of years conducting clinical trials involving stents. As we move into the drug-eluting stent realm, I am concerned with the prospect of facing a more complex regulatory hurdle to gain approval for them. Launching the trial in the U.S. was a major hurdle because of all the pre-clinical data that were required. Some companies met the rigors, and some needed to provide additional data. Sometimes it was unclear why one company was permitted to go forward with a trial while another was not. And in one instance, a company got a three-month head start over another despite having initially presented the same data — albeit presented by people who had varying influence with the FDA. When multiple regulatory branches are required to come together for an approval, it becomes very complicated. I hope that drug-eluting stents will remain a device according to the FDA, which, for all of its faults, does offer a quicker approval process for devices than it does for drugs or biologics. The FDA's biologic agency is so concerned about safety following the Jessie Gelsinger incident, that it has stifled the entire system. Hopefully, with solid physician and industry involvement, Graham Zuckerman and colleagues will put together a symposium that will attempt to determine how the process can be made more efficient. They hope to bring HCFA in to watch and learn. It seems that in government agencies, the left side doesn't listen to the right side — even when working under one director. They need to learn to communicate with one another. This will likely play out over the next five to ten years in which 20, 30, or 40 different drugs and biologics are added to ten different types of stents.