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# Device Makers, Drugmakers, and the FDA

> My children, some in high school and college by then, often sided with the critics [of the pharmaceutical industry]. They listened to my logic, but I could tell they weren't convinced, and to tell you the truth, I wasn't either.
>
> —Dr. Hank McKinnell, CEO, Pfizer[1]

In the past, Dr. Charles Rosen had looked forward to attending the North American Spine Society's annual meeting. A spine surgeon for 17 years and the founding director of the spine center at the University of California at Irvine, Rosen had attended NASS's first meeting. But in September of 2005, the 50-year-old couldn't help but feel apprehensive as he boarded the red-eye to Philadelphia. Over the past year Rosen had found himself at the center of what was becoming an increasingly bitter controversy over an artificial spinal disc manufactured by Johnson & Johnson. He had an uneasy feeling that some of his colleagues might be lying in wait for him.[2]

A device about the diameter of a quarter and made of two high-density plastic pieces sandwiched between two metal plates, the spinal disc, called "Charité," had been approved by the FDA 11 months earlier and now was being hailed by its promoters as a revolutionary alternative to fusion surgery

for severe back pain. Fusion stops the painful motion of a severely degenerated disc and associated arthritic joints by "fusing" the adjoining vertebrae so that they grow together—sometimes with the help of metal rods and screws. By contrast, the artificial disc is designed to replace the old disc. After removing it, a surgeon slips the plastic disc in between the vertebrae as if sliding a coin into a slot.

The advantage of Charité, according to J&J, is that rather than immobilizing the spine, the artificial disc lets the body move naturally. Because fusion limits the spine's range of motion, it can transfer extra stress to discs above and below the fusion site, causing them to degenerate. Charité, by contrast, allows continued motion, offering hope—though as yet no proof—that adjacent discs might be less likely to deteriorate.

But Rosen was not at all sure that the artificial disc would prove safe over the long term. Charité had been used in Europe for nearly 17 years, and after reviewing mixed data from the Continent, he was concerned that thousands of patients could wind up prisoners of their own bodies—in chronic pain, with no solution.[3] "I don't know how anyone, in good conscience, could put these things in knowing the past history and the potential for so many failures," said Rosen. "It's just money over everything else, and it's just cruel."[4]

Still, Rosen realized, he could be wrong. That was one reason why he was attending the NASS conference: he hoped to learn more.

As Rosen checked into Philadelphia's Crowne Plaza hotel and gave his name to the clerk, his premonition that Charité was going to haunt him for the next few days was realized. "Are you the Dr. Rosen who asked the FDA to recall all of those *terrible* disc replacements," asked the man standing beside him at the desk, his voice heavy with sarcasm.

"That's me," Rosen acknowledged.

The man handed him a card, identifying himself as "Mark Mintzer, Patient Advocate."

Rosen had heard of Mintzer from one of his own patients, a man who came to him after a failed disc operation left him in excruciating pain—just one of several disc implant patients who had gone to Rosen for help. Mintzer, who also had a spinal disc implant, had been far luckier. His operation had been an enormous success, and now the 48-year-old former computer consultant had become a familiar name in chat rooms for back pain sufferers, where he referred potential patients to spinal surgeons.[5]

Later in the day, as Rosen wandered through the convention center,

things only got stranger. Outside all the meeting halls, signs announced that anyone attempting to record or film the presentations would be escorted out by security guards. Rosen couldn't remember ever having seen such a sign at past conferences. The next day, at a presentation about the artificial spinal discs, the moderator reminded the audience of the warning, and indicated that at least one person already had been removed from the conference.

It was not necessary for anyone to record anything, he explained, because a CD of all the presentations would be mailed out later. "What's the difference between recording the presentations now or getting a CD from NASS later?" Rosen asked himself. He couldn't help but wonder if the conference's organizers planned to edit the proceedings, eliminating any embarrassing questions that might be asked by the audience.

The next day, he went to hear a presentation on complications following Charité disc replacements. Afterward, Rosen asked the presenter what years the disc replacements were done, and he replied, "2000 to 2002." Rosen had barely finished thanking him, when suddenly, the moderator interrupted him: "Why do you want to know? What are you getting at?" he demanded.

Rosen wanted to think that he was just being paranoid—until the last day of the conference, when he went to hear another paper about disc replacements. As he entered the large room, he noticed huge projection screens on either side of the stage. But it didn't occur to him that he was about to see his own name blown up on one of them.

At first, it seemed like a normal panel discussion. Toward the end of the session one of the last speakers began to talk about evidence-based medicine, comparing disc replacements to fusions, and acknowledging that there was disagreement among spinal surgeons as to how well the implants worked. "He was bringing up pertinent questions—I was surprised," Rosen recalls. "This is why I had come to the conference." But then, suddenly, the tone of the presentation changed.

"The speaker warned us that we had better get used to evidence-based medicine, because it's here to stay," Rosen remembers. "And he suggested that if physicians didn't deal with it, other people would bring it up. Then, suddenly, he put a slide up on the two projector screens."

Rosen expected a diagram of the spinal disc. Instead, he was stunned to see page A1 of *The Wall Street Journal,* June 7, 2005. One story was circled:

**J&J's New Device**
**For Spine Surgery**
**Raises Questions**
**Artificial Disk Aims to Help**
**Body's Natural Movement;**
**Some See Risk if It Slips**
**'Big Money Riding on This'**

Rosen recognized the headline. And he could visualize the paragraph later in the piece where he was quoted saying that the FDA's approval of the disc "puts the American people potentially at great risk for receiving operations that could fail at a high rate and result in untreatable pain and disability."[6]

Rosen remembers what happened next: "The speaker pointed to the screen and said: *'Our dirty laundry should not be aired in public.'* It was clear that he was very angry," says Rosen. "Then he told us, *'If you do that'*—and he pointed to the *Journal* story—*'this will happen'*—and a second slide popped up on the screens."

The new slide displayed a page from a class action lawyer's website. Rosen didn't recognize the attorney's name, but he did recognize his own name. There it was, in the very first paragraph. Again he was quoted saying that he couldn't imagine using the spinal disc that Johnson & Johnson was promoting. At the bottom of the attorney's webpage was the pitch to clients: "If you or a loved one suffered complications after artificial disc surgery for back pain or Degenerative Disc Disease, you have legal rights. Fill out our contact form for a free case evaluation."

Rosen groaned. Given the size of the screen, it was hard to miss his name. Although he didn't know the lawyer, he recognized the source of the quote: a story that appeared on TheStreet.com. Melissa Davis, a well-respected reporter who covered the health care industry for the online financial news site, had interviewed him about Charité, and he'd told her what he thought. "Now someone is trying to associate my name with this ambulance chaser," Rosen later told a friend, "implying that I am a shill for a plaintiff's firm, and that my criticism of the disc can be written off as unethical and financially motivated."

## "Where There Is Big Money, There Are No Disinterested People"

*The Wall Street Journal* story made it clear that the debate over the disc had become acrimonious, and that some of Charité's most vocal fans—not to mention some of its critics—had a financial stake in the outcome.

Charité's detractors pointed to patients like 52-year-old Susan Whittaker, who woke up one morning a month after a disc replacement with a badly swollen leg. Tests showed that her Charité had slipped out of its niche between the bones of her spine and become intertwined with blood vessels. During a nine-hour surgery to remove the disc, she lost pints of blood. "I'm lucky to be alive—I almost died twice on the table," said Whittaker.[7]

Ten months later, Dr. Joseph Riina, the Indianapolis surgeon who performed Whittaker's disc replacement and emergency surgery, still didn't know why her disc had slipped out of place. "We've sent films to surgeons all over the country," said Riina, who has taught other doctors how to use the device. "No one has been able to give a reason for what happened. . . . It's like hip replacement; the first ones didn't always work."[8]

Critics worry not just about slippage but about wear and tear. They point out that that no one knows how soon an artificial disc might wear out, and everyone agrees that replacing a worn disc can be extremely tricky. In June of 2005, eight months after the FDA approved the device, Dr. John Peloza, a spine surgeon in Dallas, told *The Wall Street Journal* that J&J's device would be "a nightmare to fix."

Earlier in the year, at a packed meeting of spinal surgeons in Canada, the same Dr. Peloza had attacked Dr. Fred Geisler, a Chicago surgeon who served as a consultant to Johnson & Johnson, accusing Geisler of hyping J&J's device.

Now Geisler saw his chance to reply: "Peloza is aligned with Medtronic [a competing device maker] so he thinks the Medtronic disc is better," Geisler told the *Journal*. "There is big money riding on this. Where there is big money, there are no disinterested people."[9]

But in fact, there were some disinterested parties in the spinal disc controversy—and Rosen was one of them. He had never had any financial ties to any device maker or drug company. He didn't hire himself out as a consultant; he didn't invest in their stocks.

"I'm whistle-clean—the people who want to discredit me hate that," he said a week after the NASS conference. "In the past, company reps have begun to suggest that I might consult for their company, but I always nip the conversation in the bud. Why? Because it leaves me free and clear to decide what's best for my patients. I don't want to be beholden to any company. As a surgeon, I make a fair living. I don't need to compromise my objectivity in dealing with patients. If you consult, all of a sudden you get wrapped up in that whole guilt game.

Guilt game? "You try some device, and it seems to work," he explains. "That's great. But if you begin using it—and you have a reputable name—the rep comes to you and suggests that you become a 'consultant.' Of course, you're compensated somehow . . . I just can't imagine not feeling obligated if they were paying me some huge amount of money. They're not paying you because they like you, you know—they expect you to use their product and keep using it.

"The majority of doctors aren't willing to be bought," he adds. "I counted one day—there are only about two dozen surgeons who have been really pushing the disc replacements. Many of them *do* have a financial interest—and the company has been pushing hard to offer incentives. One surgeon at the conference told me, in confidence, that a J&J rep in her town offered her $1,000 for every disc that she implanted. He told her that they would list it as some type of fee for consulting. She refused—she's not going to use the disc. But she was scared. Like me, she was also very discouraged. We both found the whole meeting to be about industry and profit, not doctors and data."

Johnson & Johnson denied the allegation that one of its reps offered a surgeon a bounty.[10] But stories of kickbacks to spine surgeons are not limited to J&J. In 2001 a lawsuit brought by Scott A. Wiese, a former sales representative for J&J rival Medtronic, accused the company of trying to persuade surgeons to use its products with offers of first-class plane tickets to Hawaii and nights at the finest hotels. Some of those lucrative consulting contracts, the suit claimed, involved little or no work. Medtronic denied the accusations in the lawsuit, which it settled in 2002 for an undisclosed amount.

In interviews with *The New York Times,* two other former Medtronic employees confirmed the outlines of Wiese's story, revealing that Medtronic's sales representatives routinely offered enticements to surgeons to use the company's hardware, including visits to a strip club in Memphis. The former employees said they had spent as much as $1,000 per doctor for a night on

the town, and a document provided by one of them listed about 80 surgeons who had consulting agreements with Medtronic that paid as much as $400,000 a year.

"It's a business deal," confided one of the employees, who declined to be named because he still works in the medical device industry. "It takes money to make money."[11]

## NASS—A Secret Society?

By the time Rosen got back to the University of California at Irvine (UCI), he wasn't just discouraged—he was angry. The controversy was turning ugly, and personal. He had heard that his name was coming up in NASS subcommittee meetings: "Who is this guy?" one doctor asked. "What's his game?" Someone on the subcommittee was assigned to call one of Rosen's colleagues at UCI to check him out.

On the Web, someone spread a rumor that Rosen was "in cahoots" with Jim Cramer, the former hedge-fund manager turned TV host, suggesting that Cramer was shorting J&J and paying Rosen to talk down the device. Rosen had never spoken to Cramer and doesn't even watch the show.

At UCI, Rosen received full support from his colleagues. No one was troubled by the fact that he spoke his mind. Many agreed with him. Everyone believed that he had a right to his opinion: without open debate, medical science could not advance.

With that in mind, Rosen sat down to write a letter to the speaker at the NASS conference who had displayed the slides of the *Wall Street Journal* story and the plaintiff's attorney's website: "You mentioned at NASS that our 'dirty laundry shouldn't be aired in public,' " Rosen wrote. "I was unaware that NASS is a secret society . . . Certainly you cannot suggest that I not provide my honest and fact-driven opinion when someone asks me in an interview. [You are welcome to] debate my opinions with hard facts and data," Rosen added. "However, I find it inappropriate that you endeavored to publicly humiliate me based upon the use of public information."

## Behind the Scenes: The FDA Panel Meets

Looking back on his experience at the conference, Rosen still isn't certain how he became the villain in this story. "The irony is that I got embroiled in this only because I wanted to *use* the disc," he explains. "I'm not a social crusader. It's just that I had been following the development of the artificial disc for 10 or 15 years, and I thought it might be suitable for some of my patients."

But before experimenting on patients, Rosen wanted to do what he calls "due diligence": "In my position, I want to make sure I know everything about a new device before I try it." So, in January of 2005, he sat down to read the 300-page transcript of the 2004 meeting where the FDA's Orthopaedic and Rehabilitation Devices Panel considered the application for Charité's premarket approval.

Rosen read the minutes of the meeting twice—and was disturbed by what he found. First, the clinical trial of 275 patients lasted only two years. Second, in the trial Charité had been compared to an outdated fusion procedure that was still in use when the trial was designed but not by the time Charité was approved. But what was most startling was that the results for the first 71 patients in the trial were not counted when deciding whether or not to approve the device. Although this first group represented roughly 25 percent of the patients in the trial, their outcomes were reported separately on the grounds that these early subjects were "training patients."[12]

The physicians were "just getting their feet wet," with those first 71 patients, Michael Courtney, project manager of the FDA's orthopedic branch, would later tell Rosen, explaining that surgeons implanting the device faced a steep learning curve.

"Just getting their feet wet?" asks Rosen. "How do you tell the child of a man who is now disabled that the doctor operating on his father was 'just getting his feet wet'? The arrogance of that . . ."[13]

Meanwhile, at the FDA panel meeting, J&J's representatives acknowledged that the rate of "adverse events" was higher among the training patients. For example, one patient had lost 1,800 cc of blood during the operation—"and that's a lot of blood." Rosen notes. "Put it this way: 1,000 cc is a liter—we're talking almost two liters of blood. What I would like to know is, which vein was cut and how? What was the problem with the ap-

proach? That's what I need to know so that I don't have the same problem if I decide to implant one of these discs."

The benefits of the disc also seemed ambiguous. Even among the later patients, 13 percent experienced "no change or an increase in pain" while 12 percent reported only "some pain relief" after the operation—which is to say that when it came to reducing pain, the implant proved, at best, marginally more successful than the fusion procedure it was supposed to replace. And since the long-term success of the operation remained unknown, it was, by definition, riskier.

Nevertheless, the FDA approved Charité—in large part because the agency had set a very low bar for approval. J&J was not required to show that Charité was superior to the outdated fusion procedure, only that it was "not inferior"—a standard that insures that the marketplace will be crowded with me-too devices which may not be better, but are almost always more expensive than the products they replace.[14]

Reading through the transcript, Rosen also discovered that approval was not, as advertised in most press reports, "unanimous." Two of the eight voting members on the panel had initially moved to postpone approval: they believed that a two-year trial did not provide adequate information on the sensitive device.

At the hearing, Charité's defenders countered that a two-year trial was sufficient because the disc had been used in Europe for nearly two decades. But when Rosen investigated further, he found that the disc's track record abroad was sketchy, at best. A 2003 article in the *European Spine Journal* summed up the state of the research: "Despite the fact that these devices have been implanted for almost 15 years . . . there are currently insufficient data to assess the performance of total disc replacement adequately. . . . Total disc replacement seems to be associated with a high rate of reoperations, and the potential problems that may occur with longer follow-up have not been addressed. Therefore, total disc replacements should be considered experimental procedures and should only be used in strict clinical trials."[15]

The high rate of reoperations posed the greatest problem. Charité was designed for younger patients: the ideal candidate, everyone agreed, would be in his midforties—which meant that at some point, the device might well wear out and have to be replaced. But no one knew how long it might last—10 years? 15 years? 20 years?

During the hearing, Dr. Paul McAfee, a consultant with J&J with a finan-

cial interest in the product, was candid: "I hope they will last 40 years. I tell my patients to look at the LeMaire data [from France], which goes back 11 years—which is pretty good" he added. But "honestly, to talk to the patients, 10 years is a pretty good outcome."

Rosen was shocked. Ten years would be pretty good? As other speakers acknowledged, if a surgeon was forced to go back in to try to replace the disc, he faced what one of the panel's experts described as a "potentially life-threatening operation."

"The problem is scar tissue," Rosen explains. "When you first implant a spinal disc you have to enter through the abdomen and navigate around the iliac veins and arteries, the major vessels that move blood throughout the body, in order to get access to the spinal column. The approach is done from the front of the body because the disc is in front of the spine. But after the initial operation, it's much harder to go back in. Scar tissue sets in, and it's very difficult to move the major veins and arteries to gain access to the spine. They can rip open—you can't imagine how quickly the whole wound fills up with a liter or two of blood.

"In a virgin operation, you can find the tear and fix it," he adds. "A second time, it's hidden by the scarring. By the time you find it, the person could be dead. We're talking about a couple of minutes here."

After hours of discussion, debate, and questions, one member of the committee finally took a stand: Dr. John Kirkpatrick, associate professor of orthopedic surgery at the University of Alabama, moved that the panel recommend against approving the device without more data. Before making his motion, Kirkpatrick pointedly reminded the panel of "a recent editorial in the NASS *Journal* discussing the fact that there are a number of spine surgeons who will do things on patients that they would never consider for themselves. This reminds me of what the FDA's purpose is," Fitzgerald added: "First, to protect the public."

Dr. Maureen Finnegan of the University of Texas Southwestern Medical Center, seconded the motion. Earlier in the all-day discussion, Finnegan had made it clear that she did not think there was enough data to approve a device that was going to have to last for years.[16] Responding to Finnegan's comment, five of the voting members of the panel concurred.[17]

But now Sally Maher, an attorney representing the device industry, jumped into the discussion. Noting that she was not a voting member of the panel, Maher declared that, nonetheless, "I have to take exception, Dr. Kirk-

patrick, to what you're saying. I have some deep concerns that if you tell a company they can't launch something for five years after they have started developing it, you're going to put a stop to new product innovation in the medical device or the orthopedic world. And I'm wondering why you feel that that's more appropriate than having a postmarket study, where you can follow the device and look at what's happening after it comes to market."

Immediately, two voting members of the panel weighed in, agreeing with Maher. One cited the 17 years of clinical evidence from Europe—skipping past the fact that this data was less than encouraging. Another complimented J&J on having "gone out of its way to document every complication that has occurred," apparently unperturbed by the number of complications.

Now Dr. Finnegan was on the defensive: "I'm not sure that some of the panel members understand that just because we say [that we're not recommending approval] that doesn't mean this is going into the closet. 'Not approval' means that, at the present time, the panel is not comfortable with all of the data. . . . It just means that certain things have to be done before the FDA makes a decision . . ."

But clearly, other members of the panel were swayed by the argument that delay might dampen J&J's "spirit of innovation." Earlier, Dr. Choll Kim of the University of California, San Diego had agreed with Dr. Finnegan: "This is a complex device," said Kim. "It's the first of its kind and designed to last for a long time, and we can't get at that question [of how long it will last] until we wait."

Now, however, Kim seemed to have changed his mind: "I think by requiring much longer follow-up, [we] will deter companies from being able to produce these innovative materials—the burden will be too onerous," Kim declared.

And so, when it came down to a vote on Kirkpatrick's motion to delay approval, six panel members backed off. Once again citing extensive European experience with Charité, the panel voted 6 to 2 against postponing approval.

Ultimately, the group compromised, and voted unanimously to recommend approval—with the understanding that after bringing the device to market, J&J would have to meet a list of conditions which included five-year follow-ups on outcomes for patients in the clinical study, and mandatory training for surgeons who wanted to implant the device. Dr. Fernando Diaz, a professor of neurosurgery at Wayne State University, emphasized the need for intensive training: "Of all the things we do in spine surgery, this is going

to be the one that will require the most supervision, monitoring and critical analysis."

J&J agreed, and when the device came to market, the company set out to train 3,000 physicians in the first year. "Before we make an initial sale to a physician, we tell him that he has go to our two-day training course," explains William Christianson, vice president for clinical and regulatory affairs of DePuy Spine, the division of J&J that produces Charité.[18] "The first half is a lecture, emphasizing selecting the right patients for the procedure, complications, and how to get reimbursed. The second half is hands-on training using animals. First the surgeons watch the procedure, then they do it themselves. They all do one operation, and they take home a CD-ROM."

But is one operation enough to become proficient? During the FDA trials, J&J considered the first five patients at each site "training patients." Meanwhile J&J consultant Dr. Paul McAfee cautioned surgeons that anyone planning to implant Charité faces a "steep learning curve."[19] Five training patients multiplied by the 3,000 surgeons who went home with J&J's CD-ROM means that up to 15,000 patients could find themselves lying face up on that learning curve.

Mark Mintzer, the patient who had a successful implant and now helps other patients find surgeons, is concerned: "I see a wave of patients going to inexperienced surgeons," Mintzer confided in the fall of 2005. "These surgeons are telling patients that the implant is little different from a fusion—and they've done hundreds of fusions. In fact the implant is very different. These doctors are misrepresenting their experience."[20]

Perhaps, rather than training 3,000 physicians in one year and sending them out to operate on thousands of patients while they "get their feet wet," it might have made more sense to limit the number of surgeons doing the operation to a small number who were involved in the original clinical trials. Their hospitals could be designated "centers of excellence" for disc replacement. And in those centers, experienced surgeons could begin training both their own students and physicians from other hospitals who had time for more than a one-day hands-on session.

But, as Rosen saw it, the problem was not just that thousands of inexperienced surgeons might do irreparable harm as they practiced on their patients. As he reread the transcript, he kept coming back to expert testimony offered by Dr. David Polly, chief of spine surgery at the University of Minnesota, reminding the panel that it was "inevitable" that over time some

discs would have to be replaced, or, in the language of spine surgery, "revised":

"These revisions will be due to infection, dislodgement, malposition and eventually to wear or wear debris," said Polly. "It is imperative that implanting surgeons understand the difficulties associated with revision procedures and that these revisions are potentially life threatening," he added. "They must then ask themselves if they are prepared to undertake such revision cases. If they are not prepared to do so, then they must ask themselves if they ought to be implanting the device [in the first place].

"I know that my . . . regional referral center will be facing these difficult revision cases whether we ever implant a single device or not," he concluded, "and I expect this will be a daunting task."

Polly was not a voting member of the panel. He had been sent to the hearing by Medtronic, one of J&J's rivals, to add his expert opinion to the discussion. "Medtronic paid my expenses, and I think their concept was to have me say a series of negative things. But I wasn't willing to say that the disc shouldn't be approved," Polly explains. "I was willing to say that once the disc was implanted, replacements would be a serious challenge—and I said that.

"I think Charité is 'okay,' but I don't think it's perfect," he adds. "Will some things go wrong? Absolutely. Will some people will die? There have been two deaths since the disc came on the market. The next generation of 'follow-on' devices that companies are developing right now will be better," says Polly. "But somebody has to be first."[21]

## "Trade Secrets"

After reading the transcript of the FDA panel's deliberations, Rosen was still undecided as to whether he should try the operation. He wanted to know more, and late in January of 2005, he contacted both the FDA and J&J.

Rosen was particularly interested in more detail on the "adverse events" that the first 71 patients in the two-year trial had suffered. Seven percent needed a second operation (vs. 5.4 percent of later patients); 33.8 percent suffered severe neurological pain (vs. 16.1 percent in the later group).

To Rosen's surprise, the FDA told him that if he wanted in-depth information, he would have to file under the Freedom of Information Act. Rosen did that and was informed that his request had been denied. According to

the FDA's Michael Courtney, the results could not be released because they were "trade secrets."

Rosen appealed: "I am concerned that the initial results of the procedure as reflected in the 71 patients may be bad," he explained. "The public has a right to know whether this is the case or not. I, as a spine surgeon being asked to put these artificial discs in, have a right to know. I also have a right to know in order to handle the possible failures that may come to me."[22]

With that end in mind, Rosen began exchanging letters with William Christianson, vice president of clinical and regulatory affairs for DePuy Spine. Christianson forwarded summaries showing the percentage of patients who suffered problems such as "neurological pain"—but again, no detail. Were they still in pain after they healed from the surgery? Why had some patients needed a second surgery? Rosen was frustrated. He could try to avoid these outcomes—but only if he had some clue as to what went wrong. He wasn't going to operate in the dark.

"I chose not to respond to his request," Christianson explained in the fall of 2005. "I thought he was being unreasonable . . . And given his negative characterization of Charité [in the press] I thought that [if he had the information] he wouldn't give us a fair shake."[23]

When asked, in the same interview, whether patients who experienced "neurological pain" were still in pain months after they had healed, Christianson explained: "We checked the patients at 6 weeks, 3 months, 6 months, 12 months, and 2 years. At each point, some patients reported pain. We added them all up and the total was 33.8 percent in the trial group—and 16.1 percent in the later group."

The next question seemed obvious: "What share of the patients in either group were still experiencing neurological pain at the end of two years?"

Christianson refused to answer: "If I tell you that," he said, "you'll want to know how many experienced pain after one year."

This was true. But wouldn't any prospective patient want to know how many patients were in agony a year later?

"We gave that information to the FDA," said Christianson. "We do not have to release it." He was correct. Legally, the level of detail Rosen was asking for is considered proprietary information, and neither the FDA nor the company is required to make it public.

And to be fair, even if Rosen had that information, he still could not be certain whether Charité's benefits would outweigh its risks over the long

term. But he would be in a much better position to outline the immediate risks when describing the operation to a prospective patient.

## The Risk of Being "Left Behind"

By the fall of 2005, more than 3,000 of J&J's spinal discs had been implanted. Although only two of the nation's eight largest insurers had agreed to pay for the operation, some hospitals were willing to absorb the cost of the $11,500 device. Earlier in the year, Dr. John Boockvar, chief of neurosurgery at Wyckoff Heights Hospital in Brooklyn, told Dow Jones Newswires that his hospital gave him permission to implant the device even though insurance would not reimburse "because it was important to be on the leading edge."[24]

Patients who read favorable reports of Charité online or in the press were beginning to demand the operation. "Some doctors say they're worried they will lose business if they don't offer the Charité option to patients," *The Wall Street Journal* reported, quoting Dr. Bernard Guiot, director of the spine program at the University of South Florida. "There's a feeling that it isn't adequately proven, but there's anxiety about being left behind."[25]

As for Rosen, he had no plans to use Charité: "Based on the evidence we have, I don't think it works," he said. "I like to do the newest things in spine surgery, but I'm interested in practicing evidence-based medicine—and we don't have the evidence."

Not everyone agreed. In the fall of 2005, Cedars-Sinai hospital continued to plug the procedure both in radio ads and on its website. There, a 1,400-word advertorial for Charité managed to avoid using the word "risk" even once. Instead, the Beverly Hills hospital assured prospective patients that the "revolutionary" spinal implant was "routine and safe."[26]

By then Dr. John Regan had performed some 200 Charité operations at Cedars-Sinai with what he described as a "90% success rate." And he agreed that the procedure is "routine and safe—most of the time." Much depends on both patient selection and the skill of the surgeon, said Regan: "I wouldn't want to see every spine surgeon in the country doing this operation—but then I wouldn't want to see every spine surgeon in the country doing many spine operations."

Regan knew the procedure better than most. "I helped develop the technique and some of the surgical instruments used to implant the disc," he ex-

plained. As a result, he has received royalties from J&J. Although he declined to divulge just how much J&J paid him, Regan insisted that the royalties had not influenced his professional judgment about the procedure.[27]

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## Drugs and Devices: Prices and Profits

The story of the Charité disc captures the secrecy, the scientific uncertainty, the financial pressures, and the potential for conflict of interest that clouds the development, approval, and marketing of new drugs and medical devices in the United States.

The amount of money at stake is staggering. In 2006 drugmakers and device makers will take in well over $300 billion—or roughly 15 percent of the nation's health care dollars.

The prescription drug industry tends to downplay the cost of its products, pointing to government reports which suggest that drugs account for roughly 11 percent of health care spending. But in fact, that figure represents only those drugs sold directly to consumers at pharmacies and other outlets. (See pie chart on page xii: "What Are We Paying For?") Hospitals, doctors, nursing homes, and other health care facilities also buy drugs, and when those purchases are included, spending on prescription drugs alone could hit $270 billion to $280 billion in 2006.[28] Add on the $36 billion that hospitals and other health providers will lay out for devices such as spinal discs, stents, and artificial hips, and the total tab for prescription drugs and devices approaches $310 billion to $320 billion.[29]

And in recent years spending on drugs and devices has become the fastest-growing component of health care costs, with outlays for drugs alone doubling between 1995 and 2003, thanks to a combination of higher prices (driving 58 percent of the rise), plus greater demand.[30] Over that span, prescription drug prices jumped by an average of 7.4 percent a year—almost three times the inflation rate of 2.5 percent.[31] In 2004 spending on prescription drugs rose another 7.2 percent, with pharmaceuticals accounting for nearly one-quarter of the total increase in the nation's health care bill.[32] Meanwhile, Americans popped more pills: from 1993 to 2003 the number of prescriptions purchased climbed by 70 percent while the U.S. population grew by only about 13 percent.[33]

Over the same span, the device industry took off. From 1993 through 2003 the industry's average revenues rose by an eye-popping 23 percent a year.[34] Looking ahead, as bionic boomers begin to replace body parts, the market for everything from artificial knees and hips to cardiovascular devices like defibrillators and pacemakers is likely to snowball—assuming that boomers can afford all of that hardware.

Just as Americans shell out far more for prescription drugs than the citizens of other countries, we also pay a premium for devices. "Europeans spend an average of just $1,270 for an artificial hip—or about one-fourth of what Americans spend," points out Sanford Bernstein analyst Bruce Nudell.[35] Stents that sell for roughly $1,500 in Europe command $2,200 in the United States.[36] And spare body parts are fast becoming luxury items: by 2005 a single screw used in spinal surgery fetched as much as $1,600, while the latest in artificial knees cost close to $10,000.[37]

Why are prescription drugs and devices so expensive in the United States? Manufacturers argue that Americans must pay dearly because in other countries, where governments regulate prices, consumers pay too little. Without U.S. dollars, the industries' supporters argue, drugmakers and device makers would not be able to cover the cost of research and development. "Implicit in this claim is a kind of blackmail," former *New England Journal of Medicine* editor Dr. Marcia Angell observes. "If you want drug companies to keep turning out lifesaving drugs, you will gratefully pay whatever they charge. Otherwise, you may wake up one morning and find there are no more new drugs."[38]

The threat is absurd. The truth is that the pharmaceutical industry spends approximately one-and-a-half times as much on marketing and sales as it spends on research and development.[39] If manufacturers slashed their bloated ad budgets, they could accept lower prices for their drugs without touching R & D.

Drugmakers themselves know that they are spending far too much on promotion. As Sanford Bernstein stock analyst Richard Evans pointed out in chapter 2, they've reached a point of diminishing returns. "Up until 1998—and for many companies through 2000—you were being paid to hire that next sales rep; you were being paid to do that next consumer ad," Evans explained. "You were generating returns for your shareholders by doing that. It is a strategy that worked. After 2000, however, even industry insiders privately admitted that billions were being wasted."[40]

But no company wanted to be the first to cut back on advertising and risk losing market share. Drugmakers, after all, are public companies with shareholders who demand an immediate return on investment. And with the pipeline of truly innovative drugs drying up, marketing has become the heart of the business. Struggling to meet Wall Street's expectations, the industry has begun to focus on producing copycat versions of already popular drugs that are all but certain to win quick FDA approval. But it is not always easy to persuade consumers and doctors to pay more for a product that is—at best—only a little better than its rivals. This may help explain why Big Pharma's promotional spending jumped by nearly 20 percent in 2003, according to *Bloomberg News,* while outlays for R & D rose by just 7.1 percent.[41]

Wall Street also drives the industry's pricing decisions. On this point, Hank McKinnell, chairman and CEO of Pfizer, is refreshingly candid: "Defenders of the pharmaceutical industry typically trot out a standard reason why prescription medicines are as expensive as they are: because the drug companies need to recover the high costs of research and development." But "it's a fallacy to suggest that our industry, or any industry, prices a product to recapture the R & D budget," says McKinnell. "Business doesn't work like that. Those are 'sunk costs.' In other words, we spent the money, and it cannot be recovered no matter what we decide to do with pricing. . . .

"If we don't use sunk costs to determine the price of medicine, how do we decide what to charge?" he asks. "It's basically the same as pricing a car, a consumer product or an appliance. *What will it take to sustain investors' confidence in the risk and rewards of an industry?* . . . If we don't generate sufficient income in the eyes of our investors . . . they will shift their capital to companies that can put it to more productive use, our stock will go down, and we'll have less capital with which to work." (emphasis mine)[42]

One drug analyst, who prefers not to be named, elaborates. "Pharmaceutical companies use price increases to fill earnings gaps left when the patent on a successful drug expires." In the fall of 2005, he pointed to AstraZeneca as an example of a company "that has put prices up on a number of its key products in the last six to nine months—5 percent here, 6 percent there, sometimes more—to meet an earnings target set by the company to impress investors." It is a policy that draws criticism in certain quarters, he adds. "There are populations—and I'm not just talking about the Third World—but within the United States, who cannot afford these medicines."[43]

Nevertheless, as McKinnell points out, manufacturers must jack up

prices to sustain profit margins. And investors who sock their savings into prescription drugs have become accustomed to very plump margins. From 1995 to 2002, pharmaceuticals took first prize as the nation's most profitable industry, reporting earnings that ranged from 13 percent to 18.6 percent of sales each and every year. Put those numbers in context: over the same span, the average Fortune 500 firm posted earnings that averaged just 3.1 percent to 5 percent of revenues. Granted, in 2004 drugmakers fell to third place (trailing "mining, crude oil production" and "commercial banks"), but even then, earnings equaled 16 percent of sales.[44]

Meanwhile, less fortunate Fortune 500 companies contributed to Big Pharma's fat margins as they bought drugs for their employees, creating what Dr. Jerry Avorn describes as "an unlikely and unsustainable economic arrangement that costs the other 98.5% of American businesses dearly. . . . For some large companies paying the drug bills of employees and retirees now consumes fully a quarter of their entire outlay for health care."[45] Put simply, by 2005 GM just couldn't afford to keep Pfizer's investors in the style to which they had become accustomed.

Even while drugmakers set records, in recent years large device makers have managed to do even better. In 2003 the industry posted net margins of almost 20 percent.[46] Like the pharmaceutical industry, the device industry is driven by Wall Street, says Dr. John Cherf, a knee surgeon at a specialty hospital in Chicago who also consults with other hospitals. Cherf, who has a business degree as well as an MD, understands how Wall Street works. Investors who bet on a medical device company know that they are taking a gamble—many devices will never come to market—and so they expect a commensurate reward.

Device makers have pulled out all the stops to meet investors' expectations, pricing and marketing their products as aggressively as any drugmaker. "They do what they're supposed to do—they're supposed to be wizards at sales and marketing, and they have done a marvelous job," says Cherf. "They've brought some incredible technology to the table, and they've made a lot of money. It's a wonderful story. But," he acknowledges, "it's probably not sustainable.

"Their margins are very, very high," Cherf explains, "and there is great price discrimination. We pay more than anyone around the world for the exact same thing. And at a time when the federal government is struggling to pay for Medicare, states are struggling to finance Medicaid—and other play-

ers in the health economy are not doing well. It just can't continue." In fact, these days, Cherf reports, hospitals are losing money on many implant procedures. "Studies that look at inpatient orthopedic departments show that only one in 10 is profitable, and the rising cost of devices is one of the big reasons."[47]

## The Real Reason Prices Are So Much Higher in the United States

Large device makers would be hard-pressed to claim that they require 19 percent profit margins in order to cover the cost of R & D. Indeed, the largest sector of the medical device business, the $18 billion orthopedic implant industry, sinks just 6 percent of sales into developing new devices.[48]

In other words, device makers, like drugmakers, charge a pretty penny for the products they sell in the United States, not because they *must* (to recoup the enormous investment that they're making in scientific research), but simply "because they *can,"* says Kaiser Permanente CEO George Halvorson. *"And, ironically, because they can, they must."* (emphasis mine)

Halvorson explains: "Imagine what would happen if the CEO of a multinational pharmaceutical company suddenly announced, 'We are now charging unfairly high prices in the U.S. So starting Monday, I am going to bring our U.S. prices down 50 percent to align them with prices in Europe'?"[49] The executive's career might last slightly longer than a Cedars-Sinai radio spot promoting spinal discs.

Virtually every other developed nation regulates or negotiates prices for health care products, either by setting reimbursement rates for new drugs based on how they compare with existing products (Japan), capping profits (Britain), putting a ceiling on total spending (France), or insisting that once a product is on the market, prices cannot increase faster than the general inflation rate (Canada).[50] In the United States, by contrast, drugmakers and device makers are free to price their products at whatever the market will bear. And when it comes to a lifesaving pacemaker or a much-needed hip, what the market will bear can be unreasonably high—not to mention arbitrary.

Kaiser Permanente's CEO explains why: "Although the United States supposedly has a market-driven health care economy . . . basic and fundamental value-based market forces are blunted here." Halvorson illustrates

his point by imagining how a drug company might set the price for a new arthritis drug in a country where it had to negotiate directly with the government. (One could envision the same scenario if Medicare were allowed were allowed to bargain with drugmakers to secure the best price possible for seniors.)

" 'We'd like two dollars a pill,' the manufacturer's salesperson might tell the minister of health.

" 'What good does the drug do?' the minister [or Medicare] asks.

" 'Well, it reduces arthritis inflammation.'

" 'Fine,' the minister [or a panel of physicians representing Medicare] responds. 'How much better is it than the old inflammation reduction drug we have now that costs us ten cents a pill?'

" 'Well,' the manufacturer replies, 'our tests show the new drug reduces pain 5 percent better than your current drug.' "

At that point, Halvorson, observes, classic market forces come into play. Value becomes relevant. Is a 5 percent improvement in pain relief worth a 2,000 percent increase in price?

" 'Sorry,' says the minister. 'Two dollars a pill isn't a good deal. We'll just keep using the old drug.'

" 'Let's not be hasty,' the manufacturer's representative might reply. 'Two dollars is just our American retail price. We can do better. How about 50 cents a pill? Would you buy them for your patients for 50 cents?' "

Halvorson envisions the health minister rejecting what would be a 500 percent markup for a 5 percent improvement in care. Ultimately, he imagines the manufacturer settling for 25 cents. Alternatively, the company might turn down 25 cents, and the drug would not be sold in that country.

"Market forces would keep it out," says Halvorson. "What market forces? A decision by the actual payer (in this case the government or Medicare) that the price of the drug exceeds its perceived value.

"By contrast," says Halvorson, "look at how that same drug manufacturer would set a price when that same drug is introduced in the United States. First the manufacturer would arbitrarily set a price, a highly profitable price." Then a division of attractive and highly trained salespeople armed with gifts ranging from doughnuts to bonus airline miles for frequent prescribers would descend on doctors' offices.[51] Meanwhile the company would run ads in various consumer and medical magazines touting the drug. Halvorson envisions the ad copy in *Time* magazine:

*Pain Away—proven in clinical tests to measurably outperform every other available painkilling drug for arthritis. . . . Pain hurts. We can help. We're on your side. Pain Away. You need it.*

"The actual and minor 5 percent pain level improvement statistic would not typically show up in the drug company ad," says Halvorson, "and certainly not as 5 percent. The typical reference would be that it is 'measurably better.' " Nor would the ad mention price.[52]

Of course some reformers argue that if Medicare and other insurers raised co-pays on overpriced drugs, individual consumers would no longer be seduced by such ads. Instead, price-wise consumers would exert market pressure by choosing the cheaper product. But how could consumers know that the new product was only incrementally better? In most cases, even the savviest patients would be hard-pressed to find the head-to-head evidence needed to compare similar drugs and devices.

For, as we saw in chapter 2, drugmakers prefer to test new products against placebos. And as in the case of the Charité disc, the FDA often demands no more than proof that the product in question is "no worse" than what is already available. The newest knee is not tested against the best already on the market. This leaves it to the individual consumer to cut through the ambiguity surrounding the risks and benefits of various potions and spare parts. One can imagine a patient asking himself: "Am I more depressed because I switched back to the cheaper pill—or am I just imagining the difference? Would I be better off with J&J's spinal disc, or the newer one, which is supposed to last longer—but has been on the market for only nine months?"[53]

Should the government intervene? Many Americans would be loath to see Washington's bureaucrats negotiating drug prices. While the loss of an arthritis pill that is only 5 percent more effective might not cause anyone great hardship, past experience with Beltway bean counters suggests that the government might shut the door on some truly valuable products, especially if those products would be of benefit to only a small percentage of voters.

But many taxpayers might feel comfortable if a panel of disinterested doctors represented Medicare in meetings with manufacturers, insisted on head-to-head outcomes research whenever possible, and then negotiated how much Medicare would be willing to pay for a drug or a device based on value—much the way FDA panels of physicians approve products. Except

in this case, it would be essential that the doctors doing the bargaining have no financial interest in the company or its rivals.

Yet, as discussed in chapter 7, the Medicare prescription benefit bill negotiated behind closed doors at the end of 2003 specifically prohibits Medicare from bargaining for the kind of bulk discounts that the Veterans Administration wins. As a result, Medicare must fork over at least 50 percent more than the VA pays for half of the top 20 brand-name prescription drugs sold to seniors.[54] And because the complicated new law "forces the federal government to underwrite the costs of all marketed drugs, regardless of their clinical or economic value," the Medicare prescription benefit bill "seems destined to channel more and more dollars into the costliest (and hence most aggressively marketed) products," observes Dr. Jerry Avorn.[55]

Admittedly, the 2003 law does allow private insurers and pharmacy benefits managers (PBMs) that contract with Medicare to negotiate prices with drugmakers. But the bill does not require that any savings from these negotiations be passed on to Medicare's enrollees. And on this score, the pharmacy benefit managers' record might best be described as unsavory.

Traditionally, PBMs like Caremark Rx and Medco Health Solutions have acted as intermediaries for large employers and insurers by hammering out discounts from manufacturers. But the PBMs have consistently refused to reveal both the size of these rebates and any other payments that they may be receiving from the manufacturers—leading to well-founded suspicions that they were not always passing along discounts. PBMs also have been fined for taking kickbacks from drugmakers in return for steering consumers to pricier products.[56] Their track record illustrates the folly of thinking that the best way to avoid gouging in the health care marketplace is to hire one for-profit company to keep an eye on another. Too often, they find common interest, as one hand washes the other.

But that is only the first reason why Medicare would be better off eliminating the middlemen and negotiating directly with manufacturers. The second is this: with 29 million expected beneficiaries, Medicare has the clout to go up against Pfizer or Johnson & Johnson. By contrast, the HMOs and PBMs allowed to bargain with manufacturers under the new Medicare law represent much smaller buying blocks, giving them far less leverage at the negotiating table. "The discounted prices that even the largest HMOs win are seldom, if ever, anywhere near as low as Canadian retail prices," says Kaiser Permanente's George Halvorson.[57]

## Device Makers, Surgeons, and Secrets

Much has been written about the pharmaceutical industry's shortcomings. Hard-hitting books like Dr. Jerry Avorn's *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs;* Dr. Marcia Angell's *The Truth About the Drug Companies: How They Deceive Us and What to Do About It;* and Katharine Greider's *The Big Fix: How the Pharmaceutical Industry Rips Off American Consumers* offer vivid portraits of an industry that, critics say, has become a vast marketing machine, far more interested in protecting the bloated sales of overpriced products than in protecting the patients who use those products. There is no need to reprise those stories of greed and recklessness here.

Though, in fairness to the industry, it is worth repeating Dr. Jerry Avorn's reminder that "Even though the proportion of revenues [that pharmaceutical companies] spend on research is not as large as their self-congratulatory television commercials imply, it is still true that billions of dollars are committed by the best companies to important biomedical investigation; they hire excellent scientists, from basic organic chemists to clinical specialists, to try to discover important new products and bring them to market. Even if too much of the industry's prodigious cash flow is diverted away from research and spent on marketing or on the development and protection of trivial 'me too' products, we still need to preserve that core of scientifically useful work . . . *In a way, we need to protect the companies from themselves—or more precisely, from domination by their marketing departments."* (emphasis mine)[58]

That said, it seems time to devote more attention to device makers. Less has been written about the medical device industry, in part because it is a smaller (though increasingly powerful) sector of the health care economy, and in part because consumers are rarely aware of the spiraling cost of devices. When a stent maker doubles or triples the price of its product, the markup is hidden in the hieroglyphics of a hospital bill.

But by 2005 hospitals were beginning to question just how sky-high prices for a stent or a knee are set—and who is setting them.

Although hospitals pick up the tab for devices (and then pass it on to insurers and patients), when it comes to picking a brand, surgeons usually call the shots. And they have little incentive to be cost conscious. Quite the opposite: insofar as the surgeon often has a close personal and/or financial re-

lationship with the device maker and its sales rep, he may well be reluctant to haggle for the best possible price.

Begin with the personal relationship: "The sales rep is my friend," declares Dr. John Cherf, the Chicago knee surgeon with an MBA. "The device companies hire people who are gregarious, high energy, and fun. And in the operating room, they help my staff." Cherf tries to keep an eye on how much his surgical center is paying for devices, but "you don't want to bite the hand that feeds you," he says. "You don't want to be too brutal."[59]

George Cipolletti, cofounder of Apex Surgical, a company that focuses on joint replacement products, agrees that the manufacturers' reps are technicians, trained not just to sell products, but to assist the surgeon's staff in the OR: "The rep can help get a surgeon out of a jam," explains Cipolletti, who once oversaw knee implant research for Johnson & Johnson. "Operating room staffs are not always reliable. There are times when, in the middle of surgery, the shift changes and you get a new scrub nurse." At that point, a rep who knows the sequence of the instruments the surgeon needs can be an invaluable aid. "In general, the rep is very well versed in how to use the device," says Cipolletti. "He can give the surgeon options: 'If this isn't working, try this . . .' "[60]

And the sales rep has every reason to steer surgeons toward his company's newest, costliest products. Reps work on commissions that run as high as 10 percent to 20 percent, and the salesman can make as much, if not more, from an operation as the surgeon. But to do that, the company salesman needs to tend to his friendship with the physician. In an interview with *The New York Times,* one former sales rep confided that he often paid the doctors' assistants $200 a case: " 'It was a bonus the surgeon didn't have to pay with his own money,' said the rep, who insisted on not being identified because he still worked in the industry and feared retribution."[61]

Clinching the connection, the surgeon may well have financial ties to the company itself. Morgan Stanley stock analyst Glenn Reicin caused a stir at Harvard's 5th Annual Alumni Healthcare Conference in November of 2004 by outing some of the most common arrangements. Reicin offered several examples of ties that bind, beginning with the case of an implant maker paying physicians $1,000 to complete a questionnaire that requires only 15 minutes of their time. Alternatively, a company may offer a surgeon as much as $1 million dollars a year to train his peers in how to use particular devices—with the understanding that he use only the company's products. In a third

example, Reicin described an orthopedics medical practice that wants to expand its research capacity by hiring a fellow. So it establishes a not-for-profit foundation to fund a fellowship. One of the medical device companies sponsors the fellowship, which carries the company's title.

"Are these [arrangements] appropriate or not?" Reicin asked.

One member of the audience cut to the chase: "We need to define the doctor as an intermediary, not a customer. The patient expects the doctor to be his or her fiduciary representative."[62]

Not long after the conference, *HBS Working Knowledge,* a weekly online publication produced by the Harvard Business School, summed up Reicin's talk: "The medical device arena—so green in venture capital money, yet so gray in areas of conduct—may prove tempting to [New York State attorney general] Eliot Spitzer if companies don't reexamine their own selling models, and soon."

In his talk, Reicin underlined just how green the sector has become. " 'We see a shifting of funds from the pharma sector to devices,' he explained. 'A couple years ago, there was a trillion dollars in market capitalization in the domestic pharma sector and only $300 million or so in the medical device sector.' " But "more recently," Reicin explained, "investors have been concluding that the drug business is riskier than the franchise model of medical devices, because drug patents eventually expire. It is true that medical devices have a very quick product cycle," *HBS Working Knowledge* noted, "but, Reicin said, device companies also develop lasting relationships with their customers and create sustainable franchises. . . . 'The relationships between the doctor and the rep are very cozy,' Reicin added."[63]

The *HBS Working Knowledge* piece, titled "Trouble Ahead: Ethics and Medical Devices," would prove prescient. Four months later, federal prosecutors subpoenaed three orthopedic implant makers—Biomet, Stryker, and the DePuy unit of Johnson & Johnson—seeking "any and all consulting contracts, professional service agreements or remuneration agreements" with orthopedic surgeons dating back to January of 2002.[64]

The probe came after years of spiraling prices. From 1991 to 2004, these implant makers boosted the price tags on their products by 132 percent, according to *Orthopedic Network News.* Over the same period, Medicare increased payments for joint replacement by just 16 percent.[65]

Orthopedic implant makers are not the only device makers who have sparked interest at the Justice Department: in October of 2005, the nation's

three big makers of implantable heart devices—Medtronic, the Guidant Corporation, and St. Jude Medical—acknowledged that they, too, had received subpoenas. According to Medtronic, the subpoenas sought information related to possible violations of federal antifraud and antikickback statutes, which prohibit payments or "provision of benefit, if any, to anyone in a position to recommend purchases of" pacemakers and other cardiac devices.[66]

Defending financial ties between manufacturers and surgeons, Dr. Stuart L. Weinstein, president of the American Academy of Orthopaedic Surgeons, argues that since doctors are intimately involved in developing new devices and techniques, "there have to be these close relationships between surgeons and industry." And when surgeons consult, they must be paid for their time.[67]

But when relationships between physicians and manufacturers are shrouded in secrecy, one can't help but understand why hospitals are uneasy. Hospital officials at Louisiana State University Health Sciences Center in Shreveport, for instance, say that they were startled to discover that Sulzer Medical had agreed to pay Dr. William Overdyke, an assistant professor at the center who oversaw knee replacements, $75,000 a year to consult on product design while also "promoting and educating other surgeons" on the virtues of Sulzer products. Though officials might have wondered why, from 2000 to the middle of 2001, whenever a patient needed a spare part, Overdyke and the residents he supervised used one made by Sulzer—especially since, before signing with Sulzer, Overdyke and his residents usually used products made by Wright Medical Technology. (At that time, Overdyke had a contract with Wright.)

Another clue that the hospital missed: around the time that Overdyke became involved with Sulzer, one of the hospital's distributors, MD Medical, also changed its representation to Sulzer. A founder of MD Medical would later become Dr. Overdyke's wife.

Overdyke insisted that Sulzer's knee was the best available, and he was never accused of directly profiting from using Sulzer's implants. But state investigators would determine that he had violated Louisiana's ethics laws, which forbid state employees from doing business with companies when they have financial ties with the companies in question. Ultimately, Dr. Overdyke was hit with $100,000 in fines, though if he had not worked for a state hospital, he probably never would have been punished. As R. Gray Sex-

ton, the counsel for the state's ethics board, observes: the case "involved conditions routinely tolerated in private hospitals across the nation."

Not only are hospitals often unaware of financial ties between device makers and surgeons, many hospitals are hazy on just how much they are paying for devices—and whether they are paying more than the going market price. Traditionally, device makers have viewed pricing as a trade secret, and as a result, prices are "all over the lot," industry insiders say. Indeed, the cost of a given device might vary by thousands of dollars from one hospital to the next. In the New York area, for example, one hospital paid $8,000 more for a DePuy hip than a competitor, according to a recent survey by the Greater New York Hospital Association. "[There has] almost been a black box around what people pay," Timothy Glennon, an executive with the association, told *The New York Times*.[68]

Recently, the hospital industry has begun to fight back. Realizing that secrecy helps drive prices skyward, hospitals have begun to call for a free exchange of information. Some have turned to consultants like Amerinet and MedAssets, which provide information about what other hospitals are paying.

But these efforts at transparency "are drawing fierce resistance," the *Times* reported in September of 2005. At that point Guidant, the nation's second largest manufacturer of cardiac implants, had sued two consultants, accusing them of sharing confidential price information. One of the consultants countersued, alleging Guidant has tried to buy doctors' loyalty with consulting agreements and other kickbacks. Each denied the other's charges.[69]

Presumably, Guidant would be among the first to denounce the idea of government regulating device prices. Waving the flag of free market competition, device makers uniformly insist on their right to charge what they wish, and "let the market" decide if the price is right. Yet by refusing to disclose what it is charging other hospitals, Guidant makes it impossible for a buyer to make an informed decision.

## Exploiting the Erosion of the Alliance Between Hospital and Doctor

Nevertheless, hospitals have been reluctant to question the devices surgeons choose, in part because it's important that a surgeon use the device that he

knows best, and in part because hospitals know that surgeons operating at their institutions could easily take their patients elsewhere. As a result, hospitals have been paying an average of $5,200 for a knee and $6,000 for a hip, says John Cherf, while Medicare reimburses the hospital just $10,000 for the entire operation. "They shouldn't be paying more than 35 percent of that $10,000 for the device itself," he adds.[70]

Not surprisingly, Blair Childs, an executive vice president with the device makers trade group AdvaMed, objects to the notion that hospitals are being gouged: "Physicians are a very discriminating customer," Childs told *The New York Times*. "It's not like you're selling to a bunch of stooges."[71]

A surgeon himself, Cherf is not suggesting that doctors are easily duped, just that they're not terribly concerned about the economic problems of the hospitals where they operate: "The device industry has done a brilliant job of exploiting the erosion of the traditional alliance between hospital and doctor," he says.[72]

As we saw in chapter 2, that alliance has been tested by the pressures of a competitive marketplace where health care dollars are scarce, and both hospitals and doctors struggle to protect their own interests. Surgeons, in particular, complain about difficulties scheduling operating rooms and delays between surgeries that cost them billable time.[73] For their part, hospitals have tried to make it illegal for surgeons to build their own surgical centers, saying that specialty hospitals skim much-needed business from community hospitals.

Cherf sides with the physicians: "Hospitals need to understand who their customer is—the doctor who admits patients. Hospitals should make surgeons' lives better," says Cherf, adding that surgeons have legitimate complaints about error rates and inefficiencies at general hospitals. "I operate in a specialty surgical center where just two languages are spoken: neurosurgery and orthopedic surgery," says Cherf. "General hospitals should be building more of these 'focused factories' themselves. If they're too expensive for one hospital to finance, maybe three or four should get together to build the facilities surgeons need. But today, general hospitals are still too entrenched in the single 'big box' theory."[74]

Cherf may be right that for too long hospitals have ignored surgeons' needs. Certainly, letting scrub nurses' shifts change in the middle of an operation seems less than supportive.

Today, however, hospitals are trying to make amends as they reach out to

enlist doctors in their fight against exorbitant and erratic pricing. In 2005 Aurora Health Care, for example, recruited Dr. Steven Kaplan, a prominent Milwaukee surgeon, when it realized that the cost of artificial hips and knees was eating up 80 percent of what Medicare paid the hospital system for an entire joint replacement surgery.

First, the hospital system needed to hire a consulting firm to figure out how much it *should* be paying for implants. Then it persuaded Kaplan to become its "physician champion." After looking at Aurora's books, Kaplan tumbled to what was going on. "In most of the cases, the implant rep in the operating room was making more than the surgeon," says Kaplan. "When I was able to point that out to other doctors, they were ready to listen. . . . I had the right selling tools."[75]

In exchange for the surgeons' cooperation, the hospital system began to offer doctors extra support in the form of designated orthopedic teams in the operating rooms and educational programs for implant patients. The collaborative effort worked: with the physicians' help, Aurora was able to bring the average price of a hip down from $8,000 to $4,300.

In the process, Aurora negotiated the cuts with every one of its vendors, so orthopedic surgeons still had access to their favorite devices. "We supported an 'all-play' program with the understanding that, if the vendors decided not to play [and offer the discounts], we would exclude them," explains Ken Peterson, vice president of systems logistics management for Aurora's 12-hospital system. "All of them ended up playing."[76]

"It's going to be a win-win situation for everybody—except the implant companies," says Kaplan. But "they've been winning for a long time."[77]

Hoping to enlist more doctors in their campaign to contain runaway device prices, some hospitals have begun to discuss sharing savings with their surgeons. In 2005 HCA, the nation's largest for-profit chain, sought federal approval for a "gain-sharing" plan that would encourage its orthopedic surgeons to select less expensive devices by giving them 10 percent to 20 percent of the dollars saved.

Predictably, the idea of gain sharing has sent both the device industry and its investors into a swivet. "This will probably start a whole new round of investor fear regarding the medical device industry and its ability to maintain healthy pricing," said Morgan Stanley stock analyst Glenn Reicin, referring to the Hospital Fair Competition Act of 2005, sponsored by Senators Charles Grassley and Max Baucus.[78]

Apex Surgical's George Cipolletti objects for other reasons: "Gain sharing is no different from a surgeon getting a check from the manufacturer," says Cipolletti. "Money is still driving the surgeon's decision when he picks a device. Doctors think about too many different things," Cipolletti adds. "I want them to get back to making medical decisions based on what's good medicine."[79]

## The "Best Knee"

Cipolletti has a point. Just as a sales rep may sell a surgeon on the most expensive device, whether or not it is best for the patient, gain sharing may tilt him in the direction of the least expensive, without the doctor even being conscious of his bias.

The uncertainty surrounding most new devices makes it very difficult to sort out motives. As Cipolletti acknowledges, the difference between an older product and a new, improved version can prove elusive. "If you talk to a statistician, he'll tell you that if you already have a knee that is giving good results 90 percent of the time, and you're trying to improve on it with a knee that will give equally good results 95 percent of the time, you'll need an enormous amount of patience to prove the difference."[80]

In truth, "there is no such thing as a 'best knee,' " Chicago knee surgeon John Cherf declares. "Three things make for a successful operation: (a) selecting the right patient for the right operation—that's 10 percent of it; (b) selecting the right device—that might count for 5 percent; and (c) surgical technique—that's 80 percent to 85 percent of it. The human input is critical," says Cherf. "Think of it this way: if you gave Tiger Woods 20-year-old golf clubs, and gave me the newest clubs, he'd still kick my butt."[81]

Even Cipolletti, the device maker who oversaw knee research at J&J, agrees: "90 percent of success is determined not by the device itself, but by how good the surgeon is at implanting that particular device—how much experience he has with it. If you were having knee surgery, that's what I would tell you to ask the surgeon."[82]

"I'd hate to say that medical devices are commodity products," adds Cherf, "but there is not a lot of long-term data differentiating their products. If manufacturers are raising prices on the newest devices claiming that they're better, there should be a warranty."[83]

Yet, as Kaiser Permanente CEO George Halvorson points out, few medical researchers would be willing to risk betting their own money on their newest products or procedures. In some cases, he reports, when health care plans have been asked to cover a new, as yet unproven treatment, they have said: " 'Try it. If it works, we'll pick up the bill. If it fails, then it's your cost, not ours.' "

Researchers virtually never take the bet because they "know that most research fails," says Halvorson. "So having their personal incomes tied to the actual success of their unproven care isn't at all attractive. There is some irony in the fact that the same researchers who enthusiastically extend hope to individual patients are, almost without exception, far too practical about the actual value of their experimental care to risk their own income."[84]

Nevertheless, manufacturers must "constantly roll out new products—and promise superior results—in order to justify the premium prices that have made them so profitable in the past," observes TheStreet.com's Melissa Davis.[85] "A lot of technological innovation serves shareholders more than patients," says Stan Mendenhall, the editor and publisher of *Orthopedic Network News*.[86] FDA data support his assertion, showing that most orthopedic devices approved in recent years gained clearance through the agency's 510(k) process for being "substantially equivalent" to items already available. Since 2000 the big orthopedic implant companies have gained regulatory approval for just five hips and one knee that qualify as "breakthrough devices."[87]

Despite the lack of hard evidence that a high-end knee is better, surgeons often want to try the newest, most sophisticated products. After all, as spine surgeon Dr. Bernard Guiot points out, "nobody wants to be left behind." Meanwhile, patients themselves frequently are convinced that what is newest must be superior.

Yet the industry's detractors argue that device makers are merely creating the illusion of success by keeping outcomes data under wraps and avoiding head-to-head comparisons.[88] "Industry is proposing new designs and new technologies almost every day—with increasing costs—and no real progress has been made," Italian physician Paolo Gallinaro wrote in the journal *Orthopedics* in January of 2005. "We all agree that scientific advances" often involve "taking a small step forward," Gallinaro acknowledges. "This means that we also must take the risk of occasionally taking a small step backwards. But haven't we taken too many steps back and only a few forward?" He points out that each of the materials used in hip joint replacement surgery has its

drawbacks: "Highly cross-linked polyethylene shows 'wear and surface cracking' when examined by an independent bioengineering laboratory. Metal-on-metal raises concerns due to hypersensitivity reactions, and ceramic can break.[89]

"If this is state of the art, why is our attention to the aforementioned problems diverted to new acrobatic toys like 'building a ship in the bottle,' i.e., minimally invasive surgery [MIS]?" he asks. Instead of constantly inventing new procedures, Gallinaro suggests, we should concentrate on improving the devices already on the market.

Yet from a marketer's point of view, new ideas are essential. And certainly, the idea of "minimally invasive" (or mini-incision) hip replacement sounds attractive. One would think that smaller incisions would mean fewer infections and fewer complications—and this is exactly what industry-sponsored research suggests.[90]

But an independent study conducted by orthopedic surgeons at Stanford University Medical Center who received no grants or support from industry found no significant benefits to MIS. Instead, the study—published in *The Journal of Bone and Joint Surgery* in 2004—revealed that the patients who received MIS faced "a significantly higher risk of wound complications" and were more likely to experience poor implant positioning and fit.

The researchers were concerned: "If other studies of the mini-incision technique also show more component malposition and more serious postoperative complications than the standard-incision technique, then the long-term results of the mini-incision arthroplasty may be jeopardized," they wrote. "Until the safety and efficacy of mini-incision total hip replacement are confirmed in the peer-reviewed literature by other investigators, we are concerned about the widespread use of the technique." In 2005 other studies of minimally invasive hip replacement published in the same journal continued to emphasize "catastrophic complications," while indicating that, at least over the short term, MIS seemed to offer no benefit in terms of post-op outcomes.[91]

Wall Street analysts took note. "During the past several years, Zimmer [Holdings, the world's largest manufacturer of knee and hip implants] has cast itself as the minimally invasive surgery company," Morgan Stanley's Glenn Reicin noted in January of 2005. But "we believe concerns may arise regarding high complication rates and poor outcomes for those patients undergoing MIS single-incision hip replacement."[92]

Critics like Dr. Gallinaro suggest that rather than crowding the marketplace with new products and procedures, device makers need to consolidate what they already know, pulling the information together into databases that would let doctors and patients compare long-term outcomes. Such databases, called "registries," are commonplace in most developed countries. By tracking actual failure rates, they throw a spotlight on problematic devices so that they can be identified and avoided. Sweden established the first registry in 1979, and this, researchers say, may be one reason why the failure rate of joint replacement in Sweden is half what it is in the United States.[93]

Some industry insiders argue that Americans would never submit to being listed in a registry because it would mean giving up their right to privacy. But in Sweden no one is forced to sign up. Patients have a choice—though the vast majority agree to enroll because they realize that down the line, if there is a problem with the device, the registry gives doctors an easy way to track them down. In the United States, by contrast, orthopedic surgeons complain that they have limited access to long-term scientific data. Despite repeated recommendations to start a joint registry here, the United States doesn't have one—largely because device makers don't want one.

"Since new products are not necessarily better than brand X, you have to hype them right," Cipolletti observes mildly. "If you actually have outcomes research, it's much harder to do that."[94]

The lack of a registry demonstrates how the culture of secrecy that permeates the medical device industry, shrouding both pricing and financial relationships between manufacturers and surgeons, extends into an area that threatens patient safety. Manufacturers are reluctant to hold their products up to the spotlight because they are afraid of exposing their flaws—even though they know that, in some cases, those defects may prove deadly.

## Patient Safety and Wall Street's Imperatives

On a balmy March day in 2005, two college students were riding mountain bikes through the red rock canyons outside Moab, Utah, when Jessica Lemieux, who was riding ahead of her boyfriend, Joshua Oukrop, "heard him call out, 'Hold on, I need to . . . ' When she turned, he was already falling backward, his bike tumbling on top of him," *The New York Times* later re-

ported. Before she could begin to take in what was happening, he had stopped breathing.[95]

When Oukrop's physicians at the Minneapolis Heart Institute Foundation learned of his death, they were stunned. Four years earlier Oukrop, who suffered from a genetic heart disease, had had a defibrillator, a device that uses jolts of electricity to shock an erratically beating heart back to a normal rhythm, surgically implanted in his chest. Joshua's physicians checked it every three months. In fact, they had examined it in January—just two months before the fatal bike trip—and found no problems.

It turned out that the device had short-circuited while trying to deliver high-voltage therapy to Joshua's heart. The FDA later reported that "the problem [was] caused by deterioration of electrical insulation in the device that can only be detected after the device has already malfunctioned. The device does not give any sign of impending failure and there is no test that predicts whether the device will fail."[96]

Joshua's defibrillator had been made by Guidant, the nation's second-largest maker of defibrillators and pacemakers. When a company official told Dr. Barry Maron, one of Joshua's doctors at the Minneapolis Heart Institute, what had happened, Maron called Dr. Robert Hauser, a senior consulting cardiologist at the institute. Hauser searched the Manufacturer and User Facility Device Experience (MAUDE) database maintained by the FDA, which contains reports of adverse events involving medical devices. There, buried in the data, Hauser found other reports from Guidant of instances in which the same defibrillator had short-circuited in exactly the same way. Neither the FDA nor the company had alerted doctors to the problem.

Maron and Hauser faced a crisis of conscience. Forty-seven other patients using the same device were followed at the institute—including Joshua's father, who suffered from the same genetic disease. "We became very concerned," Maron recalls. "We were keeping a secret not just from our patients and their physicians, but also from all the patients with the device and their physicians."

On May 12, four Guidant officials came to Maron's office. " 'What are we going to do about this?' " Maron asked. " 'We are in an untenable situation ethically and morally with our patients. How are we going to get the word out?' "

"The Guidant officials replied: 'Well, we are not. We don't think we need

to. And we don't think it's advisable.' " Guidant's emissaries expressed doubt that the patients would be able to understand the medical issues involved in determining whether or not to replace the devices.

"I said, 'I think this is the biggest mistake you will ever make,' " Maron remembers. "They said they didn't agree."[97]

They were wrong. Before the year was out Guidant would be the target of a criminal investigation.

It would turn out that Guidant had identified the design flaw in the defibrillator that Joshua used in February of 2002, a full three years before the 21-year-old died. When the company discovered the problem, it quietly made manufacturing changes in April and November of that year—*and then continued to sell devices that had been manufactured before the changes were made, while issuing no public statements about the problem or the corrections.*

The company didn't let the public in on its secret until May 23, 2005—hours before *The New York Times* published an article about Oukrop's death, headlined: "Maker of Heart Device Kept Flaw from Doctors."[98]

The day after the *Times* broke the story, Wall Street weighed in with a shrug: "It's a gray area—you can't be issuing alerts or recalls every time you have a glitch," said Thomas Gunderson, a securities analyst with Piper Jaffray. Investors also appeared to dismiss the news: the company's stock slipped just 48 cents to $73.75 a share.[99]

Meanwhile, Dr. Joseph M. Smith, the chief medical officer of Guidant's cardiac rhythm management division, explained that the company had not seen any compelling reason to issue an alert because the failure rate was very low. The company was aware of "only" 25 other cases (out of 26,000) in which the defibrillator that Joshua used had been affected by the same flaw. Smith rejected any suggestion that financial or liability concerns had influenced the company's decision, saying that Guidant believed that publicizing the issue could cause more harm than good: after all, surgery to replace the defibrillator also could pose risks.[100] What patients didn't know wouldn't worry them.

Dr. Barry Maron rejected the company's explanation: "Replacing the device poses an extraordinarily low risk—approaching zero," he said, pointing out that the devices need to be replaced every five years anyway, because their batteries wear out. Both of Joshua's doctors said that if they had known of the problem earlier, they would have changed the defibrillator.[101] At the Mayo Clinic, Dr. Robert Rea, the director of the implantable cardiac

service, agreed: "I think it very likely that we will change a lot of these devices."[102]

Joshua's father Lee Oukrop had his own Guidant defibrillator replaced less than two months after his son died. "Whoever made this decision at Guidant, I pray he doesn't have a son who this happens to," said Oukrop, who was haunted by the reassurances he gave his 17-year-old son before the implant: "I sat down with my son and I gave him my personal guarantee that this device would save his life, that he would be around for many, many years," Oukrop said. "I told him, 'You've got to have it, this will save your life."[103]

In the end, it was not up to the company to weigh the risk-benefit equation and decide what patients should and shouldn't know, says Gordon Rudd, a partner with Zimmerman Reed in Minneapolis, a law firm that handles medical device product liability cases: "If they see a pattern of a problem, they should alert patients and let patients and doctors make an informed decision."[104]

But Guidant had a compelling financial reason to keep news of the defect under wraps. In December of 2004—three months before Joshua Oukrop's death—Johnson & Johnson had announced that it planned to acquire the device maker for $25.4 billion. Wall Street matchmakers had been trying to pair Guidant with Johnson & Johnson for years. Finally, the marriage was about to become a reality. The two already had comarketed J&J's drug-coated stents, and now Guidant's pacemakers and implantable defibrillators would fill a hole in J&J's growing device portfolio.[105] Little wonder that Guidant didn't want its suitor to learn of the possible blemish on the dowry: in 2004 implantable defibrillators accounted for nearly half of Guidant's $3.8 billion in total sales.

As for J&J, the company realized that cutting-edge devices could jumpstart its earnings. The cardiac implant market was growing at about 20 percent a year, and Guidant's earnings were forecast to rise 16 percent in 2006 and 31 percent in 2007.[106] J&J was willing to pay handsomely for the opportunity. When the rumors started circulating that J&J might be ready to tie the knot with the Indianapolis device maker, Guidant was trading at $65 a share; by the time the deal was sealed, J&J had agreed to pay $76, a nice premium for Guidant's shareholders.

One can only imagine the gnashing of teeth in Indianapolis five months later when Guidant executives heard that a dogged *New York Times* reporter was digging into the defibrillator death. Over the next six months, Barry

Meier would publish some 33 stories about the failure of Guidant's defibrillator—and the fact that, for more than three years, the company had kept quiet about the problem while continuing to sell the defective defibrillators that it had in stock.

Insisting that it had done nothing wrong, Guidant tried, at first, to characterize the student's death as a tragic but rare accident. Within weeks, however, the company was forced to admit that the same type of electrical defect that destroyed Joshua's defibrillator also caused other Guidant heart devices to malfunction. Ultimately Guidant admitted that it was aware of two recent deaths involving those other devices. And since autopsies have become rare, and defibrillators are not routinely evaluated after a patient dies, Guidant would have to acknowledge that the actual rate of failure could be higher, and that the number of associated deaths might be underreported.[107]

Covering up a scandal is like ignoring a tumor—inevitably, it spreads. On June 18, 2005, Guidant announced that it was recalling some 29,000 implanted heart devices. The recalls focused new attention on other skeletons in Guidant's closet. In June of 2003 Endovascular Technologies, a subsidiary of Guidant, had pleaded guilty to 10 felony counts and agreed to pay $92.4 million in civil and criminal penalties related to its Ancure Endograft system, a stent graft device used to treat abdominal aortic aneurysms. The company admitted that it had lied to the government and hidden thousands of serious health problems, including 12 deaths.[108]

On Wall Street, in the spring of 2005, Guidant's defenders would continue to rally around the device maker, arguing that the defibrillator's failure rate was very low. There is no such thing as a "perfect device," they pointed out—and they were right. But it was the pattern of secrecy and deceit that would be Guidant's undoing.

In June investors began filing lawsuits, alleging that Guidant and its executives had purposefully covered up the problem. (Nimble investors managed to sue while simultaneously rallying 'round.) The revelation that Guidant executives unloaded millions of dollars of company stock shortly before the scandal broke didn't help their case. For example, on May 17, 2005, Beverly Lorell, Guidant's chief medical and technology officer, sold 23,300 shares for $1.71 million. On May 23, 2005, the day before Guidant made the front page of the *Times,* she sold another 22,667 shares for $1.68 million.[109]

As for Johnson & Johnson, when the *Times* story appeared in May of 2005, J&J seemed unperturbed. After all, Guidant's shares hadn't tanked—

and it's the company's share price, not the integrity of its products, that usually makes or breaks a Wall Street merger. But at the end of September, a *New York Times* story headlined, "Guidant Case May Involve Criminal Inquiry" may have given J&J pause. Two weeks later headlines indicated that J&J was "Rethinking the Cost of a Deal," and in October, five months after the story broke, Guidant shares plummeted, losing more than 20 percent of their value.[110] Evidence of short-circuiting heart implants and dead patients was not enough to drive Guidant's investors away. They didn't defect until they began to suspect that J&J might not pay a premium for their shares.

At that point, Guidant had recalled or issued safety notices on some 100,000 pacemakers and defibrillators, and had agreed to pay for replacements at $25,000 a pop.[111] Both federal and state authorities had launched investigations into the cover-up. New York State attorney general Eliot Spitzer stalked the company.

Guidant's reputation was in tatters, its financial health threatened by lawsuits, but Johnson & Johnson couldn't take its eyes off the lucrative cardiac implant market. And so in November it agreed to take Guidant to the altar after all—but at a discount. Under the new terms, J&J would purchase Guidant for $21.5 billion, or $63.08 a share, down $4 billion from the original price.

Then came a final plot twist. In December a second suitor stepped forward, and Johnson & Johnson rival Boston Scientific offered $24.7 billion for Guidant's hand. A bidding war ensued. When it was all over, a month later, Boston Scientific had agreed to pay $27 billion, $1.6 billion more than J&J's original offer, even while prosecutors widened their probe.

## Where Was the FDA?

At the tail end of the sorry story of Guidant and its defibrillator, just one loose end remains: Where was the FDA? Companies that manufacture defibrillators and pacemakers are required to file annual reports with the FDA that say how often, and why, their devices fail. And in February of 2005, Guidant had submitted just such a report, disclosing data which showed that the defibrillator that Joshua Oukrop used was short-circuiting at the rate of about one a month.

The FDA didn't issue an alert about the defibrillator until June—after *The*

*New York Times* forced Guidant to share its story with the public. At first the FDA warning was relatively mild, but ultimately the agency turned up the volume, acknowledging that while the short circuits were rare, they posed a significant risk because they could render a defibrillator useless, just when it is most needed—i.e., when the patient's heart was signaling that it was in desperate need of a stabilizing jolt.

The FDA did not make its data about the defibrillator's shortcomings public in February for the same reason that it refused to give Dr. Charles Rosen detailed information about the Charité disc: the agency labels the information it receives from companies "confidential." Noting that the FDA receives thousands of reports from manufacturers, Dr. Daniel G. Schultz, the director of the FDA's Center for Devices and Radiological Health, told *The New York Times* that it would tie up too many of the agency's resources to review the massive amounts of data sent in each year in order to sort out which should be deemed trade secrets and which could be routinely released.[112]

For its part, Guidant point outs that it made all required disclosures to the FDA, including notifying the agency in its 2003 annual report about the manufacturing change that it made in 2002. But the February 2005 report was the first of the annual filings to say that a number of devices had failed because of electrical short circuits.

Guidant also regularly sent performance reports to doctors, but in those notices the company provided only a "survival rate" for each model over time, without giving the cause of the failure. Like Rosen, many physicians believe that the warnings that they need to see are buried in the details of exactly what went wrong. It's important to know whether a device failed because its battery ran out, or because it short-circuited when it tried to save a patient's life. "Device failures that are abrupt and catastrophic are more critical than ones that happen slowly or don't interfere with life-saving functions," says Los Angeles cardiologist Dr. Charles Swerdlow.[113]

Digging for the truth, the *Times* did what Dr. Charles Rosen had done when he wanted to know more about the Charité disc: the newspaper requested copies under the Freedom of Information Act of the detailed filings that Guidant had sent to the FDA. The agency refused, telling the *Times* just what it had told Rosen: the annual reports contained proprietary information. But it would turn out that the newspaper had more clout than a physician. When the *Times* appealed that decision, the FDA, without citing a

specific reason, reversed its position in September of 2005, releasing much of the data.

"Those filings show the wide gap between the data provided to the FDA and that given to doctors," the *Times* reported. For each defibrillator model it sold, Guidant gave the agency three to four pages of information citing specific reasons for device failure, including memory problems and prematurely low batteries, and how many units failed for what reason. In its 2004 filing, for example, the company reported that over a 12-month period the defibrillator Joshua Oukrop used had suffered an "electrical short" almost once a month.

This might seem an eye-stopping fact, but it was buried in a chart on page 60 of a 96-page section of numbing numbers on Guidant's defibrillators. Some might fault the company for not spotlighting the statistic, both in reports to the FDA and in letters to doctors. Others would say the FDA should shoulder the responsibility for not sounding the alarm. "They probably didn't even read the report," said Joshua's doctor Dr. Robert Hauser.[114]

## Whatever Happened to the FDA?

In 2002 Alistair Wood, a respected clinical pharmacologist at Vanderbilt University, was close to being nominated by President George W. Bush to fill the long-vacant job of FDA commissioner. But some industry executives, along with free-market enthusiasts that included members of the editorial board at *The Wall Street Journal,* objected. When Senator Bill Frist was asked why Wood was dropped from consideration for the top post at the FDA, he summed up the opposition: "There was a great deal of concern that he put too much emphasis on safety."[115] (Dr. Mark McClellan, brother of White House press secretary Scott McClellan and son of the Republican comptroller of Texas and former mayor of Austin, got the job.)[116]

One cannot help but remember that at the daylong FDA panel meeting on J&J's spinal disc, Charité, only Dr. John Kirkpatrick stressed that the FDA's "first purpose" is "protecting the public." Other members of the panel seemed more concerned with accommodating the company's desire to get the product to market as quickly as possible.

Certainly, getting new drugs and devices to the public in a timely fashion is important—particularly those products that, unlike Charité, offer a clear

and proven advantage over older rivals. But while it is the manufacturer's job to push for early approval, it is the FDA's responsibility to hold back as it presses questions about safety. Ideally, that push and pull creates a dialogue that will balance risks and benefits. But if the manufacturer and the FDA's experts all sit on the same side of the table, no one represents the public's primary need for safety.

Over the past decade, the FDA's critics claim that the agency has abdicated its role as the public's protector. The agency's priorities started to shift, they suggest, in 1992—when the supposedly independent watchdog agency began to depend on the very companies that it regulates for a major chunk of its funding.

That was the year that the pharmaceutical industry finally succeeded in persuading Congress to pass the Prescription Drug User Fee Act (PDUFA)—a law that aimed to speed up the drug approval process by letting manufacturers fund drug approvals. In the late 1980s everyone from AIDS activists to *The Wall Street Journal*'s editorial board pummeled the FDA for dragging its heels when approving potentially lifesaving drugs. Money was a large part of the problem: the agency just didn't have the funds to hire enough reviewers. Under PDUFA, that would change.

The 1992 law opened the door to industry funding in exchange for faster reviews. Under the original agreement, drugmakers promised to give the agency $200 million in 1993—but only if the FDA spent a specified level of money on new drug approvals. For the industry this was "chump change," Dr. Marcia Angell points out, "more than offset by the added income of getting to the market sooner." But for the agency, the industry's dollars provided funding that an understaffed and underfinanced FDA sorely needed. Ten years later Congress would offer the same deal to device makers, passing the Medical Device User Fee and Modernization Act (MDUFMA) of 2002.

But rather than serving as "additional" funding, the manufacturers' contributions would become essential—and begin to dictate how the FDA spends its money. The problem was twofold: First, in the years that followed passage of PDUFA Congress cut back on its support, and the agency became more and more dependent on the dollars it received from industry. By 2004 user fees paid for more than half of the Center for Drug Evaluation and Research's annual budget of almost $500 million.[117] Second, the 1992 law stipulated that the FDA's financing of new drug reviews, adjusted for inflation, would never fall below 1992 levels (later revised to 1997 levels).[118]

Because congressional financing lagged far behind the agency's needs, over the next decade the FDA was forced to shift dollars from other programs into the review program in order to fund it at the levels that PDUFA promised. As the years passed, the agency spent more and more of its budget on getting drugs to market, and less and less on monitoring drug safety. The numbers tell the story: in 1992, the agency's drug center spent 53 percent of its budget on new drug reviews. The rest went to survey programs, laboratories, and other efforts that helped ensure that drugs already on the market were safe. In 2003, 79 percent of the agency's drug center budget went to new drug reviews.[119]

In the process the FDA has met or exceeded nearly all of the PDUFA goals. By 2003 drug approval time had been cut in half.[120] But insiders say that the FDA's independence has been compromised.

Dr. Jerry Avorn reprises a conversation between a senior FDA official and an agency scientist whose concerns about the safety of a particular drug had "attracted the ire of its manufacturer":

" 'You need,' " the scientist's boss told him, " 'to understand that the pharmaceutical industry is our client.'

" 'That's odd,' the scientist responded. 'I always thought our clients were the people of the United States.' "[121]

Even observers like Dr. Eve Slater, former senior vice president of Merck Research Laboratories, and a former assistant secretary for health at the Department of Health and Human Services in the Bush administration until her resignation in 2003, warns that "the FDA must evolve beyond satisfying the appetite of industry for faster approval." In a 2005 article published in *The New England Journal of Medicine,* Slater wrote: "We must envision the FDA as more than a counterpart to the pharmaceutical industry. It is time for the agency to realize its full potential as protector and promoter of the public health."[122]

Some say that if the FDA is going to recover its independence, it will need more money from Congress. Not everyone agrees. Avorn argues that what the agency needs more than money is a backbone. When doubts emerge about a medicine's safety, the agency needs to insist that drugmakers pay for independent tests, says Avorn. If companies balk, the agency "needs to call a press conference and issue a public notice saying, 'There are unresolved issues and we are trying to get the company to do a clinical trial and

doctors should take that into account,' " says Avorn. "The FDA has moral authority and extraordinary public relations power if they chose to use it."[123]

Inside the FDA, old hands agree. Morale is low.[124] The biggest problem, longtime employees say, is the lack of follow-up on products like the Guidant defibrillator after they have been approved. Particularly when products are sped to market, their flaws may not become apparent until tens of thousands of patients have begun using them.

Alistair Wood, the clinical pharmacologist who was once a candidate for FDA commissioner, proposed a solution to the problem in 1998 in a paper published in *The New England Journal of Medicine*. Under the present system, Wood and his coauthors pointed out, once a drug is approved for marketing, the doctors and patients assume that it is safe, unless case reports of adverse effects call that assumption into question. The problem is that there is no systematic approach to detecting problems after the product goes to market. The FDA normally relies on voluntary goodwill reporting by manufacturers and physicians.

But it is often all but impossible for individual physicians to recognize that a patient's symptoms are linked to the new drug or device—a doctor would have to see a large number of patients using the same product to recognize a pattern. And the story of Guidant's defibrillator underscores how reluctant manufacturers are to advertise adverse events.[125]

This is why Wood and his colleagues called for an independent, systematic review of products after they had been approved by the FDA. They proposed that manufacturers be required to collect data in ongoing observational studies and send that information to a drug safety board that would have enough funds to mount its own studies and hold open hearings. Indeed, the paper's authors went so far as to recommend that the board should have access to comparative data on competitors' products.[126]

Others have floated similar proposals, and by 2005 the FDA had begun to require postmarketing studies of drugs that had been "fast-tracked." But it is not at all clear that either manufacturers—or the agency—took the requirement seriously. When Massachusetts Representative Edward Markey's staff reviewed 91 studies that the FDA ordered on 42 products approved between 1993 and October 2004, the staff discovered that as of 2005 half the studies still were not done. Twenty-one of the unfinished studies had not even been begun. The oldest outstanding study had been ordered in 1996.

"It is outrageous that drug companies and the FDA have been dragging their feet when it comes to conducting required postmarketing studies," Markey observed. "They are laughing at the FDA, and sometimes it seems as if the FDA is treating it as a joke as well."[127]

## A Device Maker Lobbies the FDA

Dr. Lazar Greenfield understands why the FDA doesn't get long-term follow-up information, despite the requirements: "Once the product is on the market, that's it. The companies feel that they are in business," says Greenfield, a professor of vascular surgery at the University of Michigan.[128] He understands how the device industry works better than most, both because he's renowned as the inventor of the Greenfield filter—a device that captures blood clots before they can be transported to the lung—and because from 2003 to 2004 he became an eyewitness to the inner workings of the FDA.

On sabbatical from Michigan, Greenfield, an internationally recognized expert in vascular surgery, spent six months as a visiting scholar at the FDA.[129] "One of the reasons that I went to the FDA was to get the agency more involved in tracking long-term experience with devices," says Greenfield. "Only 1 percent of the information the FDA gets is from physicians—the rest comes from the companies themselves. And while the FDA does get adverse-event reports, sorting through them is a real challenge. They get 100,000 a year, and those are reviewed by nurses, many of whom have very little operational experience."

While at the FDA, Greenfield met Dr. Dale Tavris, head of epidemiology in the FDA device center's office of postmarket surveillance. Tavris had been working hard trying to get follow-up data from Medtronic, the nation's largest medical-device manufacturer, about its AneuRx stent graft—a device used to take pressure off an abdominal aortic aneurysm (a bulge in the wall of the main artery leading from the heart) so that the aneurysm won't rupture.

For years, the only way to treat an abdominal aortic aneurysm was by opening up a patient's abdomen. This meant making an incision from the breastbone to the navel, removing the bowels and placing them outside the body to gain access to the aneurysm, then sewing a synthetic-fabric tube in-

side the aorta in the area of the bulge. Blood would then flow through the fabric tube, making it less likely that the artery would burst.

In the late 1990s device makers developed a far less invasive alternative, using devices like Medtronic's AneuRx stent graft, a 5-inch metal-and-fabric cylinder that can substitute for the synthetic tube used in the abdominal surgery. Like the tube, the device forms a new channel for blood and takes pressure off the bulge. In this case, however, the surgeon does not have to slice the abdomen open. He can slide the Medtronic device into the body through a small incision in the thigh—a much easier procedure for a frail patient.

But while the initial operation involves fewer risks than more invasive surgery, the question remained as to whether, over time, the device might either leak or "migrate," drifting away from the spot where it was implanted. This is why Dale Tavris needed follow-up data from the manufacturer.

"Medtronic was very reluctant to provide the data," Greenfield recalls. "And much of what the FDA did get turned out to be completely unusable. Dale Tavris finally had to go back to the company and ask for raw data—before they processed it internally.

"The way Medtronic was reporting the data was really biased," Greenfield explains. "They were claiming that patients who they hadn't heard from were still living and well—that all deaths that they didn't follow up on were due to causes unrelated to the implant. They consistently sanitized the information, but Dale sorted it out, and was able to see a pattern of problems, over time."

The FDA then set out to prepare a letter to doctors comparing the risks and benefits of the new treatment to the older surgery. Studies and interviews with vascular surgeons indicated that at top hospitals, the short-term mortality rate for the more invasive abdominal surgery was low, with just 1 percent to 2 percent of patients dying in the hospital during or after the operation. At two highly regarded programs, the University of Michigan and The Cleveland Clinic, the death rate was only about 1 percent.[130] At community hospitals, by contrast, the rate appeared to be in the 4 percent to 6 percent range. But the FDA decided to use the lower 1 percent to 2 percent mortality rate to compare abdominal surgery to the Medtronic implant on the grounds that the patients in Medtronic's AneuRx sample also were treated at high-volume hospitals with good surgery results.

Setting the numbers side by side, the AneuRx stent graft looked dicey. In the initial period after the Medtronic device was implanted about 1.5 percent

of patients died as a result of aneurysms. This was no better than the mortality rate for invasive abdominal surgery at high-volume hospitals. And in subsequent years, the data suggested a 0.4 percent annual death rate for patients with the implant. There with no evidence of that rate slowing over time.

Based on the available evidence, the FDA concluded that the Medtronic device should be used on frail and/or elderly patients whose chance of dying during or shortly after the invasive surgery was greater than 2 percent. Other patients, who were at less risk of dying on the operating table, and more likely to live longer (running the long-term risk that the device would leak or migrate), would be better off undergoing the more invasive abdominal surgery.

Predictably, Medtronic cried foul. And in August of 2002, the FDA met with a group of prominent surgeons who agreed with the company. But the agency was not convinced by their arguments.

Undeterred, Medtronic continued its campaign, and 14 months later, in October of 2003, the company brought another group of leading vascular surgeons to an FDA meeting—including the then-president of the Society for Vascular Surgery. "Medtronic had helped fund the Society's aneurysm-screening program," *The Wall Street Journal* later reported. "Of the other two surgeons present, one was on Medtronic's scientific advisory board, but the other wasn't a Medtronic consultant." These experts all agreed that the FDA draft presented an unfairly negative picture of AneuRx by exaggerating the safety of the more invasive abdominal surgery.[131]

Dale Tavris, who had helped draft the FDA notice, was present at the meeting and began asking the experts pointed questions. Medtronic's champions were aggressive, and at times the meeting became "confrontational," says one FDA insider.[132] But while Tavris stuck by his guns, higher-ranking FDA officials reportedly "appeared more conciliatory and agreed to re-examine the surgical statistics."[133]

Greenfield thinks he knows what happened. "Whenever a company feels squeezed, they simply call the congressional people they support—and before long, the congressmen are on the phone to the FDA, saying, 'Back off.' "

For whatever reason, the FDA did back down. And at the tail end of 2003, more than a year after it began negotiating the language of the letter with Medtronic, the agency issued a watered-down public-health notice. The agency's most straightforward recommendation—that the devices should not be used on relatively healthy patients whose risk of dying from the ab-

dominal surgery is less than 2 percent—had disappeared. Instead, the FDA vaguely recommended using AneuRx in patients who meet "the appropriate risk-benefit profile," and went on to list factors for doctors to consider in making the decision.

Greenfield questions the objectivity of some of the surgeons who offered glowing reports of the AneuRx stent graft. "Some of these surgeons, riding the crest of the wave, were heavily involved with the company. I think it's unhealthy to have a financial involvement with a manufacturer," he adds. "I never got any royalties from my invention," says Greenfield, referring to the Greenfield filter, the device that he introduced in 1972.

In 2005 the Greenfield filter remained the industry standard and "the fact that I didn't get royalties turned out to be a decided advantage," Greenfield confides. "I could criticize things the company was doing with a device that had my name on it. Over the years, they had various engineers come along who wanted to modify it [and presumably market the 'new improved' product at a higher price]. I simply wouldn't let them do any of it until the modifications had been tested in the laboratory."

## A Device Maker Censors What a Medical Journal Can Publish

It seemed that Medtronic had won the AneuRx publicity wars—at least until the spring of 2004, when the company discovered that Greenfield, Tavris, and two of Tavris's colleagues at the FDA had written a paper titled "Aneurysm-Related Mortality Rates in the U.S. AneuRx Clinical Trial" that was about to appear in the prestigious *Journal of Vascular Surgery*. In the peer-reviewed paper, which was previewed on the journal's website, the authors used the same Medtronic data that the FDA used in its public health notice—but they returned to the conclusions of the original draft, recommending that the patients most likely to benefit from the AneuRx stent would be older, weaker patients with "higher surgical risk" and "lower life expectancy."[134]

Medtronic, believing that it had a deal with the FDA, felt blindsided.

In a letter to the FDA dated May 20, 2004, the company pointed out that it had reached an agreement with the agency about the public-health notice issued in December of 2003, and that the article about to be published in the

journal went "well beyond" the notice, "in some cases reverting to the position[s] in the initial draft . . . which we . . . believed were wrong and which were ultimately eliminated in the final version" of the notice.[135]

In fact, in the paper, Greenfield and the FDA researchers went out of their way to be fair, noting that their conclusions were based on data from "the early years of experience [with the Medtronic device] in the U.S. when users of AneuRx were going through their 'learning curve' . . . Much has been learned since then that may improve outcome of patients treated with AneuRx," they wrote in 2004. But, they observed, Medtronic stopped submitting data in October of 2002—just three years after the device was approved.[136]

"You would expect that when the company heard about our paper, they would have said, 'We have additional new data since 2002'—data that would either confirm our conclusion or rebut it. But they didn't do that," says Greenfield.

In fact, "the company has never questioned or contested the data that was to be included in the proposed *Journal of Vascular Surgery* article . . . regarding the AneuRx stent graft," Medtronic spokesman Rob Clarke explained in December of 2005.[137] Instead, "what we disputed was the data on the more invasive procedure that suggested a mortality rate of only 1 percent to 2 percent.[138]

Medtronic also claimed that the article contained "proprietary information" that the FDA had no right to disclose, though according to Greenfield "the article had been vetted for confidential information" before it was sent out. "It is not unusual for FDA scientists to submit papers for publication in medical journals," he adds. "They are encouraged to do so." In such cases "the paper goes through freedom of information, and is cleared—which is what happened with this paper. There was no proprietary information—the data in the paper was the data that had already been posted in the public letter on the FDA website. We just came to a different conclusion."[139]

Nevertheless, Medtronic's lawyers moved quickly to quash the article, firing off a leter to the *Jounal* demanding that its editors remove the preview of the article from their website and warning that "disclosure of . . . proprietary information and breach of confidentiality protections are subject to both criminal and civil sanctions which will be pursued vigorously if this situation if not remedied."[140]

In the meantime, the FDA commissioner's office became involved in the

controversy, Greenfield recalls. "There was a guy there named Dan Troy, who had become very influential in deciding the commissioner's position on various matters."

Dan Troy had become the FDA's chief counsel in August of 2001. A conservative Bush appointee and protégé of Judge Robert Bork of the U.S. Court of Appeals, Troy was a longtime foe of FDA regulation. In the 1990s he had represented the Brown & Williamson Tobacco Corp. in its effort to fend off the FDA, and just months before joining the agency, he had defended Pfizer in another battle with regulators. A *U.S. News & World Report* headline summed up his career change: "Mr. Outside Moves Inside: Daniel Troy Fought the FDA for Years; Now He's Helping to Run It."[141]

During the first two years of the Bush administration, Troy operated in a power vacuum. The FDA had no permanent commissioner, and "while the White House and Congress publicly argued over who should lead the agency it was being quietly transformed by appointees such as Troy, who needed no congressional confirmation," *The Boston Globe* observed.[142] *U.S. News* corroborated the report, saying that Troy "operated as the de facto head of the FDA" between September of 2001 and November of 2002. During that time, the magazine added, Troy held "at least 50" closed-door meetings with representatives of drug companies and others regulated by the FDA. When *U.S. News* sought records of those meetings under the Freedom of Information Act, it was informed by Troy's office that there were "no minutes, no memos, no nothing." Troy resigned his FDA post without explanation on November 16, 2004.

But in the spring of 2003, Troy was still chief counsel, and when Medtronic complained about the article that had been accepted for publication in the *Journal of Vascular Surgery,* "Dan Schultz, the acting director of the FDA's Center for Devices and Radiological Health, was told to write a letter to the medical journal requesting that the paper be withdrawn," Greenfield recalls. "He was very unhappy about this."

Off the record, Schultz told a colleague that he felt "compromised,"[143] though publicly he would insist that the FDA did not intervene in order to please or placate Medtronic. Rather, "the way in which the information was presented in the article was somewhat different from the way in which the information was presented in a previously issued public health notification," he explained. "When I was asked to take a look at all of that together, I felt that the article needed to be pulled."[144]

"These are very good people—but they're midlevel. Their hands are tied," says Greenfield who, unlike FDA employees, is free to speak his mind.

To the shock of many in the medical community, the *Journal of Vascular Surgery* did not print the article. "Since when has the FDA begun telling medical journals what they can and can't publish?" one surgeon asked.[145]

But the *Journal of Vascular Surgery*'s editors did speak out in a special editorial in August of 2004, saying that cancelling the article "in response to objections by a manufacturer of a device regulated and approved by the FDA is very disturbing." The editors went on to say that they were "extremely disappointed by the actions of the FDA and Medtronic Inc., which have prevented the publication of an article containing data that we believe are important to readers of the journal."

"As editors, we are responsible for preserving the rights of authors to communicate appropriately reviewed scientific information and for preventing corporate influence of this process," said Jack Cronenwett, a professor at Dartmouth Medical School and one of the editors of the journal. "In this case we were unable to do so."[146]

## End of an Era?

For years drugmakers and device makers have enjoyed fabulous success. Under siege, they have nonetheless warded off threats of tighter regulation, registries, caps on price increases, and imports from Canada. But despite that success—or perhaps because of it—by 2005 both industries were riding for a fall. Great success, after all, breeds excess.

"I think even the drug industry may be beginning to realize that you can't simply stomp around and do whatever you want—without consequences. People get cheesed off—demanding Canadian imports and all the rest of it," one Wall Street drug analyst observed late in 2005. "In a sense they've reaped their whirlwind."[147]

Despite the billions spent on TV ads, by November of 2005, it was getting harder and harder to sell the public on pricey products. "A lot of the demand that the industry has created over the years has been through promotion, and for that promotion to be effective, there has to be trust," said Richard Evans, a stock analyst at Sanford C. Bernstein.[148] "That trust has been lost," Evans added, referring to revelations that Merck had failed to

follow up on signs that its best-selling drug, Vioxx, led to increased risk of heart attack or stroke, while other drugmakers concealed the results of clinical trials which showed that patients who took antidepressants might run an increased risk of suicidal thoughts.[149]

Big Pharma's popular support was waning. In the fall of 2005 Merck had lost one high-profile trial, won another, and still faced a firing squad of plaintiffs' attorneys intent on winning large awards for patients who took Vioxx. Meanwhile, a Harris Interactive survey disclosed that only 44 percent of the U.S. public viewed the industry as doing a good job for its consumers—down from 79 percent just seven years earlier.[150] Even America's most popular drug, Lipitor, was under attack, the subject of a lawsuit filed in U.S. District Court in Boston, claiming Pfizer deceptively marketed the drug to women and the elderly, without proof that the drug lowers the risk of heart disease for these groups.[151]

This not to say that the industry was on the skids. Pfizer alone expected to make about $8 billion in profit in 2005 on sales of roughly $51 billion. But investors were restless. In the fall of 2005, shares of market leader Pfizer were near their lowest levels since 1997, and a broad index of drug stocks has fallen 25 percent in five years.[152]

Drugmakers had done their best to keep profits high: from January of 2000 through December of 2004 they hiked prices on 96 frequently used drugs by nearly 25 percent.[153] But during this span, they were finding fewer and fewer promising new drugs to bring to market. In the third quarter of 2005, Pfizer acknowledged that spending on research and development was down 6 percent from the same period a year earlier, and said it expected its research budget to stay flat or decline in the years ahead.[154]

Revenues already had begun to slow. In 2004, after nine years of solid double-digit growth, industry sales grew by just 8.3 percent. Some saw sluggish sales ahead. In 2005 Datamonitor PLC, a business information company, predicted that drugmakers could expect revenues to grow by an average of only 2.2 percent annually for the rest of the decade. "The pharmaceutical industry is in the process of transformation," longtime Pfizer board member Stanley O. Ikenberry told *BusinessWeek*. "We have to reexamine all the assumptions that pharmaceutical companies have made for as long as I can remember."[155]

Now drugmakers were forced to talk about cutting costs. In the summer of 2005, Wyeth announced that it was trimming its sales force. "The market-

place has changed, and frequent visits are not well received anymore," said company spokesman Doug Petkus.[156] This was an understatement. Physicians were so fed up with seeing sales reps in their waiting room that drugmakers were committing "death-by-salesman," quipped Sanford Bernstein stock analyst Richard Evans.[157] Even Pfizer reluctantly admitted that it planned to shrink its massive sales force, mainly through attrition.[158]

Some on Wall Street suggested that drugmakers could and should make far deeper cuts. "Companies have just been slavishly following what everyone else is doing," observed one drug analyst. "If you have profit margins of 25 percent—who cares how much you spend? Nobody is rigorously calculating whether they are getting return on investment."[159]

By 2005 institutional investors with enormous sums at stake were beginning to mutter that the industry should "rethink its business model," the same analyst confided. "These investors tend to be pension funds, with long-term liabilities to be concerned about. They recognize that health care stocks represent 10 percent of their assets under management," and that if share prices fall, "you could easily see that 10 percent become 5 percent." Worried that after years of aggressive marketing and pricing Big Pharma is about to "reap its whirlwind," these investors are beginning to say, " 'You can't carry along this path, or you're going to meet quite a bit of resistance.' "

"Of course, no one wants to rethink the business model," he admits. "It has worked quite well—in the sense of generating profits. But if you did think about it, you would see a great deal of waste."

For example, some investors point out that drugmakers could save millions by making intelligent use of information technology to capture data in doctors' offices. Others ask why Big Pharma is not the low-cost producer of its own products. Why is it that the generics take away its sales after a patent expires? "In any other industry, if you are the manufacturer, you would strive to make the product as efficiently as it is humanly possible to make it," says the analyst. "But pharmaceutical companies don't seem concerned with driving down their own costs"—largely because they have been able to make enormous profits without worrying about efficiency.

Further belt-tightening is in order, he suggests. "It might mean doing clinical trials in Poland, Ukraine, or South Africa—where you can do them for 20 to 30 percent less than in the United States. It might require shifting manufacturing to Singapore or India. I'm not saying any of this is comfort-

able," he adds. "But the drug industry doesn't have a divine right to comfort—any more than any other industry."[160]

Institutional investors realize that these ideas are controversial, but what is important is that it is not the industry's scolds, but rather some of its biggest investors, who are talking about radical changes in how drugmakers do business.

## Will CMS Begin to Use Its Clout?

Looking ahead to 2010, the biggest question for the pharmaceutical industry is this: how will the new Medicare prescription drug bill play out? Many see the complicated new law as a bonanza for the drug industry. Or, as a *Pittsburgh Post-Gazette* headline put it in November of 2005: "While Seniors Scratch Heads, Big Pharma Licks Chops."[161]

Others are not so sure. How many seniors will sign up? Will HMOs negotiate deeper discounts? And will Medicare finally exercise some muscle in deciding what drugs to cover?

Thanks to the new prescription drug benefit, the "federal government's share of the national drug bill will rise from 13 percent to over 40 percent," *Medical Marketing & Media,* a pharmaceutical trade publication, predicts. "The Centers for Medicare and Medicaid Services (CMS) will thus control the purse strings and have the clout to bring about major reform in the country's healthcare system. As administrator of the agency since March 2004, Dr. Mark McClellan . . . has made it quite clear that he intends to introduce rational, economic-based decision-making into healthcare."

"Let's face it," McClellan said in a Webcast on September 29, 2004, "the only way we can continue to justify the payments required for truly innovative new drugs is by generating evidence that demonstrates the benefits of these treatments and that gives patients and doctors timely and specific information about how to use these treatments with confidence that they will get better outcomes as a result."

"Enter the era of outcomes research which is already a factor in other countries, but has not yet caught a strong wind in the U.S.," suggests *Medical Marketing & Media.* "CMS will champion reforms such as head-to-head clinical trials and more robust health outcomes data. Products that prove them-

selves superior will earn generous reimbursement deals. Those products that do not stand out will be limited to receiving a small, fixed percentage of the cost as their profit margin. When competing products are deemed to be 'functional equivalents,' CMS will select the lowest cost alternative. CMS's stance on the relative worth of drugs will no doubt form a model for other payers."[162]

For CMS to begin inquiring into the cost-effectiveness of new products would require a striking shift of ideology on the part of the Bush administration. Nevertheless, as Washington struggles to pay for the trillion-dollar Medicare drug benefit, device makers, along with drugmakers must consider the unpleasant possibility that CMS will begin asking questions about value before agreeing to reimburse for new products.

Device makers also must worry about how Justice Department investigations will affect their relationships with surgeons, and whether the prospect of gain-sharing between hospitals and physicians will become a reality. "Implant prices cannot continue to spiral," Dr. John Cherf, the knee surgeon with an MBA, said in the fall of 2005. "I tell analysts at money management firms—I would sell these stocks. They're all down double digits. It is coming to an end—it is not sustainable."

Cherf is not alone. Ray Elliott, chief of Zimmer Holdings, the world's largest manufacturer of knee and hip implants, alarmed investors at a Bank of America conference in the fall of 2005: "There's a lot of bell-and-whistle stuff in this industry over the last five or six years where you got pretty good money for stuff that was pretty fluffy . . . ," Elliott declared. "If [you think] you're going to take [a device] and spray it red and add $1,000 to it and say, 'This is still the good old days,' it's not going to happen anymore."[163]

Perhaps 5 or 10 years from now, we'll look back and say that 2006 marked the end of an era for both device makers and drugmakers. In the meantime, some see the second half of the decade as the beginning of a brave new era for HMOs. In the years ahead, many of Wall Street's forecasters predict, the insurance industry's giants could wind up taking home the pot of gold at the end of the Medicare prescription drug rainbow. And at the same time, they say, managed care companies should be able to turn a nice profit by selling younger Americans on a new form of high-deductible, low-premium insurance. Optimists call it "consumer-driven health care."