RECORD, Volume 31, No. 2*

New Orleans Health/Pension Spring Meeting
June 15–17, 2005

Session 4PD
Medical and Rx Technologies—What's in the Pipeline?

Track: Health

Moderator: LISA F. TOURVILLE

Panelists: BORIS GARCIA-ZAKZUK
WINIFRED S. HAYES
LISA F. TOURVILLE

Summary: This session presents information sources used in tracking health technologies, the value of health technology assessments and clinical data typically available. It also includes the value of proactively managing emerging technologies and forecasting the financial impact to health care costs. The presentations are going to include examples of technologies expected to have a financial impact on the health care industry over the next 1-2 years and beyond. At the conclusion, attendees gain insight into the importance of proactively managing emerging technologies as well as an understanding of the critical role actuaries can play ensuring their organization is pricing and budgeting appropriately, given expected changes in the health technology pipeline.

MS. LISA F. TOURVILLE: Winifred Hayes is founder and CEO of Hayes, Inc., a health technology assessment and medical informatics firm. Ms. Hayes will talk about the identification of emerging technologies and the assessment of their impact from a clinical perspective. Dr. Boris Garcia-Zakzuk is the vice president and director of medical affairs for GenRe. He will talk about emerging technologies and their impact on medical care. I'm with Reden & Anders, and I'm going to close by talking about forecasting the financial impact of these issues.

One of the themes of this presentation is the importance of not looking at this issue from an actuarial perspective. You need the clinical perspective as you're trying to quantify the value and the impact of medical technology. It is one of the most critical challenges facing health care organizations today.

On the medical side, the impact of health technology on overall trend has varied anywhere from 0 to 2 percent in recent years; on the pharmacy side, the impact of health technology on overall trend has varied from -5 percent, all the way up to +2 percent. Combining the two together, the impact has varied from -2 percent to +2 percent. A lot of people don't think that that's a big deal. But when you're dealing with trend factors of 10 percent, and in one year it may go from 10 to 6 percent purely due to changes in emerging technologies, it's kind of important to be aware of that and understand it.

A health insurer should have a proactive process in place, an effective process that spreads across the whole continuum of departments throughout a company. It helps actuaries to forecast future medical expenses more accurately. It helps underwriters to price business more appropriately. It helps corporate finance improve the ability to hit earnings targets. It helps when it comes to rate filings, to have solid information behind rate actions. It helps medical officers to make educated policy and coverage decisions for the subscriber base, and to better set priorities and proactively develop care-management strategies. It helps benefit managers make educated benefit plan design decisions. It helps provider contractors; when you know that a new technology, a device, is entering into the marketplace, and you have an idea of what the manufacturers are saying that it will cost, being able to go into a hospital contract negotiation with that knowledge is a real benefit to you. Finally, it helps administrators to make a business case for imposing administrative controls. Often, we work with clients who will make a decision not to cover a certain technology, only to find out six months later that they've been paying for it all along. Make sure that your claims adjudication system is set up so that it's administering the policies the way that you want it to.

With that, I'm going to introduce Ms. Hayes. Ms. Hayes is an expert in device-evidence-based health-technology assessment and independent medical review. She founded Hayes, Inc., in 1989. Her business acumen helped to grow and focus the company. Today, it's a nationally respected leader in health technology assessment. Its mission is helping people to make the best health care decisions. Hayes provides accurate and timely evidence-based reports on the safety, efficacy and costs of emerging and often controversial health technologies. Hayes Reports provides a large collection of health care technology assessment information. Its topics address significant health care questions.

MS. WINIFRED S. HAYES: I have the first part of the panel presentation: the methods. Hopefully, I can make this very relevant for you. It’s the grounding for how we begin horizon scanning and the forecasting process. I want to talk about how we monitor the health technology pipeline, what sources we use, how we track a specific health technology's development in a specialty or clinical service line, and how we identify those emerging health technologies that will impact trends. In other words, how do we distinguish another “me-too” technology from real, innovative technology that will make a difference clinically and therefore impact utilization and costs? How do we assess a technology as it continues to evolve,

once it's moved into the commercial marketplace? Some technologies evolve very rapidly; others evolve over years. Finally, I will address forecasting the impact on utilization and clinical outcomes.

When we talk about health technologies, we're speaking very broadly. They include things like drugs and biologics, laboratory studies, medical devices, imaging equipment, surgical procedures, laboratory tests and assays, genetic tests and planned clinical guidelines—really, anything we do in the context of providing health care to patients. Whether it's preventive, screening, diagnostic, treatment or end-of-life care, it is considered a health technology.

Because we monitor health technologies as the core of our business, it's important that we develop methodologies that are employed in a very consistent and systematic fashion and that they accomplish what we're trying to do, which is to make sure that we pick up on and identify any health technology that is going to have an impact on clinical outcomes, utilization and, therefore, cost. We begin quite broadly, and we start by monitoring new sources that cover a very wide spectrum of activity. I'm going to give you some of those.

Another important element that I want to review with you is sources of information that allow you to focus on clinical service lines and that allow you to monitor progress that's being made in certain areas continuously. For example, one of the hot areas right now is robotics. There are sources of information that we go to, to monitor the developments in robotics as devices that assist in different surgical procedures. The third element is a survey of new clinical trial data from a variety of sources, including the peer-reviewed literature and conference proceedings. There are some clinical journals that are very important, and most of you are familiar with those journals. There are also some other sources of information that give us access to the publication of clinical journals, very broadly speaking. That is another way that we're on top of what's going on in the marketplace.

When you identify a technology of interest through all of these very broad scanning techniques, how do you figure out whether the technology has merit? Do you want to rely on one published study as a predictor of whether you think that this health technology is going to have an impact or not? Or, do you want to drill down and make sure that you thoroughly look at all sources of information about this technology in making your determination? Obviously, the latter methodology is the one that you should be employing.

I think that everybody is aware of the importance of evidence-based medicine today in health care. That is actually a buzzword, and I think that it's lost some of its meaning. Evidence-based medicine, as a term of art, refers to an approach to clinical knowledge that is grounded in scientific research. When we talk about evidence-based medicine, we're talking about judgments made and knowledge gained through a systematic review of scientific evidence. That is in contrast to relying on the opinion of a physician expert. The reason that horizon scanning

should be grounded in scientific evidence is that evidence is what really propels the process by which technologies are evaluated, tested, and then judged to be either safe and effective and ready for commercialization or not yet ready.

The Food and Drug Administration (FDA) approval process requires studies to support drugs and biologics before they enter the marketplace. Though the FDA is not nearly as rigorous with device reviews as it is with drugs, a Class III device requires scientific data to support its efficacy and safety before it is cleared for marketing. The clinical community looks to evidence as a way of evaluating whether something is effective or not. Even though it might be tempting to pick up the phone and call the neurologist that you know in a local hospital and ask him what he thinks about this latest drug for brain cancer, it's more effective and reliable to go to scientific literature and concentrate on that, because you're less likely to be misdirected by following that methodology versus the opinion of one or two physicians.

Our methodology requires that we drill down into the scientific literature when we're trying to evaluate something that we've picked up in this very broad screening process. It's very helpful to set your organization up on a number of listservs. You can design those listservs around specific clinical services lines. It's very helpful in terms of making sure that nothing is falling through the cracks in your horizon-scanning activities.

Some of the key news sources that we use to start our very broad horizon scanning include: http://www.google.com, http://ap.org, http://www.fda.gov, http://media.prnewswire.com, http://www.medscape.com/homepage, http://online.wsj.com/home/us, and selected manufacturer Web sites. A number of them are public-sector news sources. These news sources are useful in broadly scanning to identify technologies that are going to have an impact on usage going forward. *The New York Times* is another good source. You can bet that if something hits “The Today Show,” you're going to hear about it at some point in time, because it has such a broad audience that it creates demand for the product. Oftentimes, the products are not ready for commercialization, but they will get some airtime and stimulate interest.

When you've identified a technology, it's important to begin to take a look at the real merit of that technology. You want to follow a very specific process in doing that. That process includes structured database searches of medical science databases. Those structured searches use keywords and confirmation techniques that are very important to follow in a very systematic fashion.

When we begin to drill down, what makes us decide that a technology is going to have real impact going forward? We begin to take a look at the quality of clinical evidence currently available. Is it weak? Or is it robust? Is it characterized by small studies and case-series data, or do we begin to see controlled clinical trials and, in particular, randomized controlled trials? Is all of the research currently

funded by the manufacturer, or are there other sources of funding? The reason that we ask that question is that there can be bias associated with research that's funded only by a manufacturer. Early on, that's pretty typical. We begin to look at whether there are other funding sources that are brought to bear in exploring the clinical worth of a new technology. In addition to looking at the quality of research, we're looking for replication. Is all research being done by one party, or do we have other researchers across the country who are finding similar results? Is the research all yielding the same conclusion, or are there conflicting conclusions? Those are the important things that we begin to look at in predicting not only whether something will be safe and efficacious and have clinical merit, but also how far it is from commercialization. How long will it be before this product enters the commercial marketplace?

A second area that we begin to look at is: What is the target population? Sometimes, manufacturers hype their product. They may imply that the market application is a lot broader than it actually is. It's important to look at the patient indications as research is being done on a technology. Is it the whole population of people, for example, with diabetes that is going to respond to this technology? Or is it a subset of people with a particular kind of diabetes, Type I diabetics who are refractory to normal insulin therapy, for example. Most intervention applications can be narrowed to particular populations of patients. That information about disease incidence and prevalence, and, in particular, patient selection criteria begin to give you the information that you need to know within your population of insured people—those most likely to fit this profile and for which this most likely will be used. We begin to hone in on that kind of information.

The other aspect that is important is to look at the predictors of uptake on the part of clinicians and patients who want this procedure or therapy. There are a lot of things that impact uptake—things like: Is this an invasive, painful or uncomfortable procedure? Is this something that is going to be difficult for clinicians to use and interpret? Does this take a tremendous amount of skill for a physician to use, so there will be a long learning curve? It could be that there is a lot of variation in terms of performance excellence. There are a number of factors that will impact uptake, including the cost of the item and expensive pieces of equipment. Hospitals may demand more clinical data supporting its impact on clinical outcomes and more data on how this technology competes and compares with existing technology. All of those factors need to be looked at when you research information sources about a technology that you think will have an impact on trend.

You want to project the cost and commercial availability of whatever it is. When is it likely to become commercialized? What do we know about the FDA review process, if the FDA is involved? When are we likely to see it actually enter the marketplace?

Finally, you must track competing technologies, both technologies that are in use currently and those in the pipeline. We've seen many examples of the importance

of that in the recent past, drug-eluting stents being one with four manufacturers competing. One stent is already in the marketplace; others are soon to follow. It'll be interesting to see what happens in terms of the merit of one versus the others.

All technologies are not in the same class, but they may have similar applications. A good example of a technology grouping would be all of the technologies that have entered the marketplace to treat prostate disease—benign prostatic hypertrophy, in particular. There are more ways to freeze, fry, cut, etc., the prostate gland than you can imagine. It's important to begin to examine them. Is there any information that tells us that one technology is superior to another, as we begin to look at the treatment of a given disease?

Another thing that is critically important is that the investigative message should include a confirmation of facts, using at least two independent sources. Don't rely on one source. It's always a good idea to get at least two independent sources to confirm your information. As I've already mentioned, relying on expert opinion can lead you astray. Expect the developments for some technologies to be very rapid. It's important that you have a method in place to monitor the technologies that you're tracking and update information on a quarterly basis, at least.

Staffing this area involves tapping into a variety of people. Clearly, actuaries have a role in interpreting this information and applying it to trend. But I think that actuaries in this field work best in combination with clinicians. It's important that you have the kind of clinical input that you need to help interpret some of this highly technical information.

Here are some additional sources of research information:

Professional associations:

- American Medical News, http://www.ama-assn.org/amednews
- American College of Cardiology: Advocacy, http://www.acc.org/advocacy/advocacy.htm
- American College of Physicians, http://www.acponline.org/computer/ccp/bookmark/
- American Society of Clinical Oncology, http://www.asco.org

International Agencies:

- The European Agency for the Evaluation of Medicinal Products, http://www.emea.eu.int/
- Canadian Coordinating Office for Health Technology Assessment, http://www.ccohta.ca/

Portals:

- Doctor's Guide, http://www.pslgroup.com/dg/haematonews.htm
- PharmaLife, http://www.pharmabusiness.com/
- EurekAlert, http://www.eurekalert.org/

- Pharmaceutical Manufacturers Web sites

Electronic Mailing Lists:

- Google News Alert listservs, http://www.google.com/alerts?hl=en
- British Medical Journal, http://bmj.bmjjournals.com/alerts/
- Food and Drub Administration (listservs), http://www.fda.gov/emaillist.html
- SEER database

Published literature is important, including foreign journals. There are other electronic databases. Professional organizations and academic research institutions hold a lot of conferences and publish the results. Industry research initiatives include manufacturer Web sites and government clinical trial databases. Centers for Disease Control and Prevention (CDC) statistical reports give you added information on incidence and prevalence.

Here is an example of how this methodology works. A biologic called Herceptin is used to treat HER2-positive breast-cancer patients. The reason I selected it is that it's in the marketplace already; but two very important recently published studies will greatly expand its use. This is an agent that could have an impact on trend, because its use is going to be expanded dramatically. It has the potential to do many good things for breast cancer victims. It has had a dramatic impact in reducing reoccurrence. When we picked this up in the news and looked at the clinical studies, one of the compelling bits of information was that these studies were sponsored and monitored by the National Institutes of Health (NIH). They were randomized clinical trials. They occurred in different centers. They both had similar findings, and the findings were so dramatic that the NIH called a halt to the study so that all of the people enrolled in the study could benefit from the therapy. That's dramatic. That doesn't happen very often. So this truly is a major breakthrough.

As we looked for this information, we searched key clinical trials for Herceptin. We identified the actual trials. We were able to go online, look at the trial itself, look at the enrollment in the trials, look at the outcomes, look at the controls that were in place and evaluate the quality of evidence. We also went to the “gray literature,” annual meeting abstracts, and so forth. The focused review of clinical trial protocols of abstract data lets us see the patient selection criteria very clearly. For actuaries, that means that you know exactly the patient population of appropriate candidates for this therapy. That can be translated to your insured population, based on the data that profiles the proportion of people, historically, who've had breast cancer that meet these criteria.

MS. TOURVILLE: Dr. Garcia-Zakzuk is responsible for group health claims on underwriting services for GenRe Life Corp. As medical director for the group division, Dr. Garcia-Zakzuk leads the division's managed care initiatives. Dr. Garcia-Zakzuk’s unique background has allowed him to consult on group medical underwriting topics in both the United States and Latin American markets. Prior to

joining GenRe, he worked at The Travelers and at Aetna. Dr. Garcia-Zakzuk holds a degree in medicine and surgery from the National University of Colombia. He also has earned the Health Insurance Associate (HIA) designation. He's a co-chair of the Group Underwriters Association of America's reinsurance committee and a frequent speaker at its meetings.

DR. BORIS GARCIA-ZAKZUK: I will talk a little bit about the technology, the devices in particular. There are so many technologies in medical care that, on a weekly basis, we can find a conference going on any place in the country on these new tools and techniques. Something is happening every single day. It is in the news every day. There are so many things that we cannot talk about everything. Today we will concentrate on certain diagnostic tools, surgery, drugs and bioengineering devices.

On diagnostic tools, by far, imaging technology is the area in which the impact of technology is more noticeable. Computer axial tomography (CAT scan or CT scan) is very fast and produces a higher quality of baseline pictures for areas inside of the body. But at the same time, they can produce many false positives in detecting benign lesions. They are very good for detecting malignant lesions, in general, but there are a lot of false positives.

Positron emission tomography (PET scan), on the other hand, can detect little changes in cell metabolism and small cancer tumors, distinguishing them from benign lesions. Certainly, it's the best tool to detect Alzheimer's disease in the early stages. While private insurance carriers began paying for PET scans more than 10 years ago, Medicare still does not pay for PET scans. That, of course, is one hurdle for the PET scan producers to further develop the technology.

The combination of a low-dose spiral CAT scan with a PET scan effectively detects early lung cancers. Only 5 percent of small lesions in the lungs of adult smokers become cancerous. A study of the Society of Nuclear Medicine demonstrated that the combination of a CAT scan with a PET scan can save about 1,154 lung-cancer patients through more accurate diagnostics. That is without loss of life expectancy, compared with the alternative of a CAT scan, by itself. Every year in the United States, about 85,000 patients are diagnosed with non-small-cell lung cancer. If each one of those patients were managed with the combination of a CAT scan and a PET scan, versus CAT scan by itself, the savings would be around $98 million in a year, without any change in life expectancy.

Magnetic resonance imaging (MRI), as everybody knows, is one of the most expensive tools out there. There are three major manufacturers that are developing new systems for parallel and 3-D imaging. They are creating open systems, trying to make them more patient-friendly. A lot of people don't like being inside of a tube at the time of the examination. Right now, they are developing the whole-body MRI. All of these companies are working on that at the same time. When that is ready, it's going to be very expensive. Right now, CAT

scans are available for the entire body. For $4,000, people can get a whole-body CAT scan done for themselves. The reason behind that is insurance companies do not pay for those procedures. But people are buying these procedures, mainly wealthy foreigners coming to the United States.

With ultrasound, many manufacturers are aiming at the obstetric market. They are developing 3-D features. They are able to detect malformation, especially cardiac malformation, in the fetus. Surgery is being done in the uterus or via Caesarean section prior to the delivery time. There is a trend toward miniaturization. They are making these devices very small, about the size of a laptop.

With regard to X-ray technology, direct digital radiography is new. The same thing that happened with photography is happening now with X-ray. Before, you had to take the film to the laboratory to develop; you had to wait some time. It was the same situation with X-rays. You had the X-ray image taken, and then they had to pass the film through a laboratory process. Not anymore. Now it's like digital photography. They take the X-ray and results are available in seconds. They are also creating image "stitch-ins." They take several pictures of the body or a limb, and then they put them together to compose the entire body, attaching one to another electronically.

A lot of new diagnostic tools involve genetic testing. About 57,000 Americans and about 500,000 people worldwide die from colon cancer each year. DNA tests for colon cancer, developed by scientists, make the big promise of catching many cases of colon cancer instances before they become life-threatening. That information was based on a recent study publicized in the *New England Journal of Medicine*. It would reduce the need for more invasive procedures like colonoscopy, resulting in improved patient care and reducing health care cost.

For non-small-cell lung cancers, epidermal growth factor receptors are being developed. There is evidence that for the short axis of chromosomes 18, 19 and 21, some patients have certain mutations. Four different studies showed that 100 percent of the patients that have these conditions were responsive to a new drug called gefitinib. A common characteristic on these patients was that they never smoked and all of them were female. After these mutations were discovered, there was a study with gefitinib, where 250 milligrams were administered daily. After seven days, all of those patients showed evidence of cure in the X-rays. That is a dramatic event. The good thing about this one is, while it took them a long time to discover all of this, gefitinib is inexpensive. It's shown a cure for a bunch of patients that before were dying, with no treatment for them.

Medical schools are using 3-D scanners to train medical students to simulate surgical procedures. They can do the surgical procedures on a console in a 3-D image. They don't have to touch a patient and risk the liability.

Sometimes, babies are born with a cleft lip or cleft palate. In Scotland, the incidence is about one in every 650, per live birth; in the United States, it's about one in every 320. The Cleft Lip and Palate Association is using a scanning 3-D technology. They take images of the babies, and they can foretell the whole structure of the electronic imaging. They can plan the surgical procedure in such a way that the reconstructive surgery is done more successfully and the end results are better looking.

The Michelangelo dynamic scanner is a device with an aim to provide the infrastructure and tools for research into whole-body imaging for applications in the creative media, biomedical and other sectors, by deploying whole-body 3-D imaging.

The first generation of robotic surgeons already is being installed in operating rooms around the world. The da Vinci Surgical System, which is one of those more common and better-recognized in the world right now, was approved by the FDA on July 11, 2000. Before that, its cost was $1 million. Right now, its cost is $2 million. Right after the approval, the price went up. It was developed by Intuitive Surgical, Inc. It has a viewing console. The surgeon sits in a very ergonomic position and has a surgical arm unit. This surgical arm unit has three rods. One of them holds a camera, and the other two hold surgical instruments. The procedures are done via three little incisions that are about one centimeter in diameter. They insert the three probes in and, using that camera, the surgeon is able to get very close, a lot closer to the surgical field than they could do in the traditional way. In the traditional way, the surgeons are standing up and work from a greater distance. With this technology, the camera is right in the surgical area. They can see the surgical area better. Not only that, but these robotic systems have software that eliminates the tremors or sudden movements in the hands of the surgeon, preventing accident. In the United States right now, it is approved for the removal of the gall bladder. The Germans did it for the first time back in 1998. They also did angioplasties and coronary artery bypass using the da Vinci system. Instead of opening the chest around the sternum in order to do the coronary artery bypass surgery, they are making three little holes in the chest. The recovery time is a lot shorter, and the patient goes home a lot quicker. That procedure still is not approved in the United States.

The ZEUS robotic surgical system is very similar. That continues to be in the trial phase in the United States. It is approved in many European countries, but not in the States. The cost is still $750,000 for the system. As soon as it's approved in the United States, the price will likely go up. The automated endoscope system for optimal positioning was the first robotic system approved by the FDA back in 1994. It is much simpler than the da Vinci system and the ZEUS. It's, basically, just one robotic arm used by physicians to position the endoscope. Robotic-assisted microsurgery is a micro-dexterity system that was created in combination with NASA in the jet propulsion laboratory. It is designed to permit tele-manipulations of the robotic devices.

Robotic surgery is being used for hip replacements, as well. Right now, hip replacements have a ratio of about three failures of every 10 patients in the term of 10 years. With robotic surgery, using CAT scan and imaging technology, they are able to determine the precise size of the femur. Based on that information, surgeons are able to get the process for the correct size from a catalog. They put that information into the computer of the robotic surgeon, and the drilling is made exactly where it should be done without ever moving one or two degrees to the right or to the left and therefore producing complications on the patient. It's perfectly done. The recovery time is a lot shorter, reducing also the need for further surgery 10 years later when the patient is older. The future of robotic-assisted surgery will have an impact on personnel. Fewer people will be needed in the operating room.

Gastric bypass is another surgical procedure that is hitting us, especially now. It was first prescribed for weight reduction about seven years ago. Remarkable contributions have been made in that field. Techniques are different from one institution to another, and the surgery continues to carry a high morbidity rate. Adjustable gastric banding is another type of bariatric surgery. Different facilities choose different procedures. The average cost for bariatric surgery is about $26,000 per patient, not counting any complications. The mortality rate is less than 1 percent. That also depends on the facility and how many they do.

However, more than 20 percent of these procedures have complications. Those complications include intestinal leaks and nutritional abnormalities. The most common one is the dumping syndrome. Sometimes, because of the surgical procedure, the stomach becomes a tube instead of a bag. When food enters the body, it goes down too quickly. When that happens, the patients become sweaty very quickly after they eat. The blood pressure goes down, and they become faint. Because of that, they usually carry candy. When they are having the symptoms of dumping syndrome, they start chewing candy to compensate for the hypoglycemic attack. The end result is that, a year after that happens, they are in need of another surgical procedure. These procedures are more effective in the severely obese, those 100 pounds over their ideal weight.

In 1997, 23,100 bariatric surgery procedures were done in this country. In 2004, 140,640 were done. In 2005, the estimate is between 170,000 and 175,000. The growth continues, in part, because of an older population, the publicity that the procedure has gained, and the fact that some insurance companies are paying for the procedure. Still, especially in the stop-loss area, some plans do not cover the procedure. As soon as the procedure is covered, everybody wants it. Remember, we are a society that is accustomed to the quick fix, and bariatric surgery is a quick way to try to fix things.

Cryoablation uses very cold temperatures to destroy tissue. It is a new option for prostate cancer patients (especially young patients) and breast cancer patients (especially to remove benign breast tumors). The procedure could be done at the

doctor's office under a local anesthesia. The patient goes home after the procedure is done.

Radio frequency ablation on lung cancer is a new technology. There was an article on that in a recent edition of *USA Today*. Doctors are destroying tumors inside the lungs with heat, using needles. One thing that they discovered was that while they are able to get the needle in and destroy most of the tumor, sometimes there are some cancerous cells in the walls of the hole that was made with a hot needle. Now, they created what they call “smart capsules.” These smart capsules have chemotherapy drugs. They are injecting these capsules inside of the new space that they created with another hypodermic needle. The heat activates the capsules, which release the chemotherapy. In that way, chemotherapy is given very locally. The side effects are, of course, much lesser.

In the orthopedic area, Osteoset is a bone-graft substitute that is composed of pellets of calcium sulfate. It is the only one approved to be used in the presence of infection. That's great, because it actually works. The patient has the chance to recover during the presence of infection. INFUSE is a bone graft. It's the only FDA-approved bone graft replacement specifically for use in lumbar spine fusion procedures to treat degenerative diseases. In 2002, the lumbar taker fusion device (which is pretty much like a cage) was approved by the FDA. Because of this, spinal fusion has become a little bit more practical. Before, to do a spinal fusion, they had to take a bone graft from the hips of the patient. That means that you needed incisions on the hips to retrieve the bone, and then do the surgical procedure on the back. Now, instead of that, they are using this procedure.

The LTFD device was created by a company in Indiana. During the trial process, several orthopedic surgeons participated in the trial. Of course, they became very good using it. As soon as it was approved in Indiana, everybody there has the procedure done. There are three of these physicians. They only charge about $6,000 for the procedure. But the hospitals are charging for the devices on the bone graft. They are charging between $25,000 and $45,000, and the procedures are being done by the same physicians. It's interesting. If you have any clients in that area, you will notice that. And the hospitals, sometimes, are basically across the street from the physician’s office. The difference is dramatic. That's another question for hospitals. They charge what they want to, and there's no easy way to control them.

Neurosurgeons are doing amazing things with nerve rerouting. With patients that have spinal cord injuries and are not walking because of that, they are dissecting the ulnar nerve, rerouting it to the leg and reconnecting it to the stump of the nerves in the legs. Patients are able to walk with crutches, versus being in a wheelchair. The Israelis are doing nerve reconnection, and they have been doing it for a while. A lot of patients are gaining mobility in their legs. There is one physician, in particular, in Portugal that is doing stem cell transplantation. He's

taking stem cells from the nostrils and transplanting them, and the patients are starting to move their lower extremities.

In the area of drugs, a bunch of pills with different original treatments are being used now for the treatment of cancer. There is Celebrex, which was removed because of the cardiac side effects, but now it's being used for colon and lung cancer. The osteoporosis drug Bonviva is another example. The best thing about this one is that the treatment is done on a monthly basis, and the patients can take it with an empty stomach if they want. The equivalent drug to Bonviva has to be taken three times a day with food, because it causes irritation of the stomach. There was a French doctor that treated himself out of addiction to alcohol with Baclofen. After that, with clinical trials and experiments, they found that it interferes with the reward circuit in the brain, and because of that people stop drinking alcohol.

I think that the most famous engineered tissue right now is artificial skin or the bioengineered skin that is used to treat severe burn patients and chronic foot ulcers. More than 70 companies are spending more than $600 million a year to develop new products. The artificial liver is like liver dialysis. They are using porcine cells in combination with activated carbon or human liver cells grown in the laboratory to fill up these canisters. Some patients that have acute liver failure are hooked up to these machines, while their own livers recover from the acute failure. They go back to a normal functional life or wait for a liver transplant while a donor shows up. Left ventricular-assisted devices are allowing patients on the list for heart transplants to stay alive until a donor heart is available. Unfortunately, this is very expensive. Many times, for patients in the hospital that are hooked up with a left ventricular-assisted device, the time that they are hooked up ends up being more expensive than the heart transplant. A heart transplant costs $300,000 to $350,000 for all phases.

There are many scientists working on an inflatable, implantable heart with a fully portable battery pack, allowing the patient to remain mobile. We will see that in the future again. Most of the artificial hearts have failed, but work continues to be done in that area. At the Nottingham City Hospital, PRODIGITS were made for patients with hand deformities or partially amputated hands. They are artificial hands that hook up to different nerves. They can move the fingers. There are also developments in blood-pressure-regulating devices. Last summer, there was a 36-year-old woman with severe hypertension. She had a pacemaker-like device implanted and connected to the carotid artery, where we have some nerves that control our blood pressure. It's working. Because of that, she doesn't need any medication. She is wearing only this electronic device that sends electrical impulses to these centers, and it's controlling her blood pressure.

GlucoWatch was approved in the year 2003 to control blood glucose using the fluids of your body (basically from your sweat). Every 20 minutes, the device gives you a reading of your blood glucose. If it gets too low or too high, it beeps and lets the

patient know what's going on. There are more things being done with hemodialysis, trying to have a patient to do the process six times a day with a clear improvement in the quality of life. Now, dialysis machines are being sold for $13,000, in combination with a $5,000 water purifier. They are cost effective, and things could be done. Electrodes are being implanted in the eyes and ears. People born blind are able to see shapes; and people born deaf are able to hear now, due to cochlear implantations. Cholesterol testing machines are easier to use. It just requires a little stick, in the same way that glucose is tested in the urine.

In conclusion, there is growing evidence that, on average, the health improvements resulting from newer, better and more intensive treatments have been well worth the added cost. That is true for a wide range of diseases, including the improvement in survival after a heart attack. Medical advances are doing more than just keeping the elderly alive. A recent study suggests that the rate of disability among the elderly population has declined in recent years. Although primary prevention has been an important contributor, most advances in cardiovascular health care are due to innovations in mechanical treatments to improve blood flow to the heart or pharmacological treatments. Health care recommendations made by the President's Council of Economic Advisors in February of 2003 encouraged flexible, innovative and broadly available health care decisions. The private insurance industry responds more rapidly than bureaucracies to changing technologies and new innovations in products and devices that characterize the American health care system.

MS. TOURVILLE: I'm going to talk about forecasting the financial impact of emerging technologies. I intend to give a couple of examples, just a sampling of technologies to watch from a financial perspective.

As I said earlier, a proactive process helps actuaries and underwriters, finance professionals, medical officers, benefit managers, etc. The most important thing is to leverage both the expertise of the actuaries and the clinicians.

How do you go through the process? A detailed, structured process should be followed to manage the impact of emerging technologies effectively. Four key steps get repeated over and over. First, you work with somebody like Dr. Hayes. Identify the new technologies. What are they? What do we need to be looking for? Then, you make a preliminary actuarial projection, which you can't do unless you're talking to someone like Dr. Garcia to help you understand some of the clinical applications. Then, your company makes your clinical and benefit policy decisions. Are we going to cover the technology? That's the number one decision. Following that, if we are going to cover it, how are we going to handle it in the benefit plan design? Is there a copay? Is it a formulary issue? How are we going to deal with it? Then, you recalculate your actuarial projections. That's what you put into your forecasts.

You can see that there's a continuum. It's really a circular process. You end up repeating a lot of the steps. Identify the technology, research and price it. Send it through a peer review process. Adjust your pricing, if necessary. Set the coverage policy. If there are any care management strategies that you can develop to help to control the expenses, make sure that people who are truly in need of the technology are the ones who are getting it, and that there's not financial incentive to give it to absolutely everybody. Establish your benefit design. Adjust your formulary. Adjust your pricing. Go through peer review, again.

Once it actually goes live, start tracking your experience. Not only do you want to understand how quickly it's being disseminated into the marketplace, but you continue to learn. You learn from your past mistakes or past triumphs as you're forecasting. We really take this very seriously in the processes of our forecasting. We have a specific component when we tear apart trends—going back historically, as well as projecting into the future. There are the basics. There's the cost. There's the utilization. But you keep pulling the technology apart. We want to understand, historically, from year to year, the impact of that technology. Then, we can understand what that's going to do in the future.

What do we consider emerging technologies? Absolutely everything that's changing in the medical marketplace needs to be considered. You need to take into account when you're doing any kind of forecasting that there's a question of what's technically in the baseline and what's outside of the baseline. If there are technologies that are getting used more often because patients are changing their behavior, you need to account for that and forecast for it. But generally, you have a baseline change for patient behavior. We specify and forecast for many things—new diagnostic tests, new treatments, new devices, brand-name patent expirations, drugs moving from prescription to over-the-counter, changes in medical and pharmacy guidelines, changes in FDA status and new medications.

When we forecast, there are a lot of moving parts that we need to try to capture and quantify. Some of these include the timeframe for FDA approval, which alone is a moving target and can be very difficult to understand. We've had what were considered to be blockbuster technologies that were expected to get approval in three months. All of a sudden, the manufacturer pulled it. Things change continually. Monitoring that is extremely important. Understanding the patient population is also important. Who's eligible? Who would want the technology? Adoption rates among physicians are important. There's a new technology out there, but are the physicians all going to accept it right away and start recommending it to their patients? Another issue is the potential for off-label use. We see a lot of different therapies come through that the FDA has approved for a specific cancer, for colon cancer, for example, and off-label use spreads; they start using it on breast cancer, on non-small-cell lung cancer.

Barriers to patient access are relevant: Is there a shortage of whatever the technology is? You must also consider relative effectiveness of alternative

therapies, technology costs and cost to administer. You don't want to look at the cost of the drug-eluting stent alone, but take a look at the facility charges and the professional charges that would be added to that. Offsetting costs from foregone treatments is also key; if they're going to use a drug-eluting stent, obviously they're not going to be using bare-metal stents anymore. There is a very different cost structure, but there still is going to be an offsetting cost there. Emerging competing technologies are interesting. Look at some of the new technologies coming out for wet macular degeneration; I think that there are four different ones. Each one has a very different cost structure, but each one has different side effects and success ratios. The percentage of patients who are going to take each one will make a difference in your modeling.

Certificate of coverage—are you going to cover it? What's your benefit plan, the formulary? Contract negotiations—we have a technology cost that's expected, but if you negotiate differently, you're going to have a different impact. Administrative controls—of course, on the government side, the public-to-private cost shifting. The government says that it is going to pay a certain amount for a drug-eluting stent. If the manufacturer is charging a lot more than that, what do you think is going to happen on the private side?

I have a couple of examples. One of them is very simple. It's a patent expiration for Zocor. We model patent expirations. We determine the utilization for the brand name and the cost assumptions. The first step is to estimate what percentage of usage will shift from the brand name to generic. We have statistics. Different classes of drugs can have different shifting patterns. For Zocor, we used an assumption that 93 percent will move to the generic, ultimately. Utilization assumes one unit equals a 30-day supply. We estimate cost relativities between the brand and the generic.

The expected cost of generic simvastatin (what Zocor is made of) assumes a cost reduction of 25 percent in the first six months, and 50 percent thereafter. That can vary by different classes of drugs and by what happens with the marketplace. We've seen the cost drop 90 percent in the 12 months after a generic drug enters the marketplace. They can differ drastically. The assumption here was a 25 percent cost reduction in the first six months. The reason that six months is different from thereafter is because, generally, one company is awarded the exclusivity from the generic side for about six months. So there's only one competitor to the brand name. But after six months, the door is wide open. The competition really heats up, and the costs come down further.

What was the result in this one? Ultimate utilization is 57.96 per 1,000 members. The expected release date is the first quarter of 2006. That's something that can move around. You need to track that very carefully. A lot of litigation takes place, especially when new generics are entering the marketplace. Impact grades in nonlinearly over three quarters. Not only is unit cost dropping, but we're assuming the adoption rate to be 50 percent in the first quarter, 90 percent in the second

quarter, and then 100 percent thereafter. Our expected technology cost is $69. The offsetting cost—which would be the brand name Zocor—is $132. Weighing all of those things together, we get a peak per-month per-member (PMPM) result of negative 31 cents PMPM. We get negative 21 cents in 2006 because of the grading in that's occurring. Negative 31 cents occurs in 2007 and 2008. When it comes to impact on trend, it's the change in PMPM that we care about. By 2008, the impact on trend is zero.

This next example is at the complete opposite end of the spectrum from the brand-name versus generic example that I just gave. This one is dependent on contingent outcomes. This is a treatment for colorectal cancer using Avastin and Eloxatin. Initially, we started modeling the impact of Avastin. Then we add on Eloxatin at a later date. The assumptions that we've made, based on the side effects and the studies that are going on right now, are that 80 percent of the population will use Avastin, and 20 percent will use Eloxatin. We started by modeling the eligible population. We get a lot of our information from the SEER Cancer Data Set and different sources.

We estimated that 90 percent of colorectal cancers are treated using chemotherapy of any kind as the first line of therapy. We modeled based on off-label use for mortality rates from the first two years following diagnosis for patients diagnosed with breast cancer or non-small-cell lung cancer. The cost of one dose of Avastin is estimated at $2,500. Again, we don't know that for sure, yet. The next important thing is: How many doses are they going to receive? That’s where the contingent modeling comes in. You go through a lot of work to get the answer.

For the treatment regimen for advanced colorectal cancer with Avastin, research indicates that all patients will receive a minimum of six weeks of therapy, with three doses administered every other week. That's your minimum number of doses. We need to come up with an average or a median. The response rate to this regimen is 0.45. There's a 45 percent chance that a patient will continue to receive Avastin for a period of time longer than the minimum six weeks. For patients responding to Avastin, the median time to progression is 45 weeks, and the hazard ratio is 0.66. That's one of the reasons that Avastin is being considered a blockbuster. That is the survival rate, the probability that the treatment will stop a patient from moving into the next stage of cancer therapy. The median number of doses that a patient will receive is 22.55. Median time to progression is 45 weeks, administered every other week. Ignoring attrition, using all the statistics, the expected number of doses administered per patient should be 11.8. If you multiply 11.8 times $2,500, you get $29,000, ignoring administration costs, the cost of other pharmaceuticals in this regimen, any offsetting costs and costs associated with extended survival.

Obviously, we're a long way from being done, even though we've already done this much. Considering the hazard ratio of the new regimen and the one-year survival rate of the old regimen, we can calculate a weekly survival rate of 0.995 and a

termination rate of 1.0. Using these above parameters and following a standard life annuity calculation at zero interest, we arrive at a new value that explicitly recognizes attrition. Rather than the 11.8 up above, we're getting down to 10.94 as the expected number of doses. That brings the expected cost per patient down to $27,340. We still have a long way to go. We need to add administration costs, as well as costs for other pharmaceuticals that would not have been received if Avastin had not significantly improved survival and extended first-round chemotherapy. Increased costs might be incurred in the second and third rounds of chemotherapy as more patients survive to receive them. We must add the impact of off-label use, the impact of including Eloxatin and the offsetting costs.

The final result, after we've done all of that additional work, is the ultimate utilization. We get to 0.19 per 1,000 members. The expected release date for this one is the second quarter of 2002. Impact grades in nonlinearly over 18 quarters. The expected technology cost is $74,000. After including everything, that $29,000 jumps up to $74,000. The offsetting cost is $16,513. We get a peak PMPM of 91 cents. That moves through time: two cents in 2003, 16 cents in 2004, 70 cents in 2005, and 91 cents in 2006. Again, it's the change in PMPM that we're most focused on for the impact on trend.

I would like to add a couple of updates for the generic Allegra. On April 14, 2005, Barr Pharmaceuticals was granted the ability to enter into the generic Allegra market. On April 11, 2005, the company announced that the FDA had determined that Barr is entitled to 180 days of sole exclusivity. From that point on, things will change. We'll get a lot more competition.

The new meningococcal vaccine usage is going to increase significantly. I'm sure you're all aware of this one, with college students and high school students. Another example is COX-2 inhibitors—Bextra, Vioxx, Celebrex. We've been noticing that even though the utilization for the non-steroidal anti-inflammatory drugs (NSAIDs) have been dropping, overall, some of the costs were going up. We were trying to figure out why. We saw significant growth in proton pump inhibitor sales. I saw a commercial on TV in which Nexium was the “purple pill.” They advertised it as though you feel so great when you were taking it that you would be running through the fields. Now they're actually associating it with the NSAIDs and telling you that it will help reduce the stomach problems and the pain. They definitely changed their marketing and are capitalizing on it.

Finally, here is just a sampling of technologies expected to have financial impact in 2006: wet macular degeneration, hybrid Capture 2 HPV DNA Pap smear, vagal nerve stimulation as treatment for resistant depression, ultrasound for aortic aneurysm, Erbitux. Obviously, a lot of these technologies are very dependent on demographics. If you're looking at Medicare population, there is a much larger impact. Plan B, the morning-after pill or the abortion pill, is another one with results that will be very dependent on whether or not it is approved by the FDA. That's something that we're watching very closely.

MS. GAIL LAWRENCE: Dr. Garcia-Zakzuk, in your conclusion, you stated that advances in technology are worth the cost. You certainly gave some examples for which there are better outcomes with shorter recoveries. Who should make the assessment that all of that money is worth the cost?

DR. GARCIA-ZAKZUK: That's a great question. I would say that people like Ms. Tourville could make the assessment. Her company and the tools that they develop are the best processes to implement to do that type of assessment. Internally, everybody can take a look at it. Initially, some processes are more costly, but the length of the stay is shorter, the recovery time is shorter, and the chances for additional surgical procedures is lower. All of that has to be taken into consideration.

MS. TOURVILLE: One of the most important things is to get as much data as you can and take a look at the outcomes. There are some outcomes for which it's much more difficult to be able to do that. Drug-eluting stents are one great example. You need longitudinal studies. You need to look at the experience through time. There is a greater cost up front. Will it ultimately reduce costs? We should be able to see that. We should be able to track that if everything that they say is true.

MS. HAYES: I'll be a bit more controversial. I don't think that we're making decisions about the worth of any particular technology in a very consistent fashion. I think that, as a country, we haven't come to grips with the worth of the clinical benefits that new technologies bring. A lot of technologies are “me-too” technologies and don't improve clinical outcomes substantially. I think that there are some that are blockbusters. But I do believe that we're at a point in this country where we seriously need to debate the issue of what we are willing to invest in what ways to improve clinical care and outcomes, and who should make that decision. Right now, by default, it's made by a lot of different people. The federal government makes it for some Medicare recipients. Private insurers make it as part of their coverage policy determination. Private physicians make it in terms of what they recommend to patients—some of which is not reimbursed. It's made by a lot of different people, and certainly is not driven by scientific evidence, necessarily. There are a lot of things that drive it.