WHLE

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The Wharton School of Business

THE WHARTON HEALTHCARE LEADERSHIP EXCHANGE

SPECIAL FEATURE

PERSONALIZED MEDICINE: THE ROAD AHEAD

ALSO INSIDE, CONVERSATIONS WITH...

Newt Gingrich

Governor Phil Bredesen

Hank A. McKinnell, PhD

For 11 years the Wharton Health Care Business Conference has gathered together some of the top minds from across the health care spectrum to debate the critical issues facing the industry in a unique cross-disciplinary forum. Participants range from leaders in drug, device, payor, and provider organizations, to bankers, consultants, academics, and venture capitalists. The assembled conversations, panels, and speeches at the Conference are deliberately broad in scope, combining and contrasting different opinions and backgrounds from every sector of the industry, to help participants make connections and discover insights they might not find in a more narrow setting.

Last year, we sought to establish a mechanism to extend the intellectual exchange of the event's participants beyond the boundaries of the Conference itself. That instinct was the genesis of this journal, the Wharton Healthcare Leadership Exchange (WHLE). The goal of this publication, as the title suggests, is to create a forum, in print, for the exchange of ideas on the most challenging and topical issues in the health care industry today and to share that exchange with both attendees of the Conference as well as others who could not attend the event.

In our second volume of the WHLE, we have continued our efforts to share with you the opinions of the top minds in the industry. To guide the conversation, we have chosen in this issue to focus on current, challenging topics across four diverse sectors in the health care landscape: Health Care Policy, Global Health, Personalized Medicine, and India's Rise as a player in the health care landscape. To highlight the important role of the school in the health care industry, we have also included three features on the affiliates and activities of Wharton: one with an MBA alumnus, one with a member of the faculty, and one on the Wharton Healthcare International Volunteer Project.

As we address the contemporary challenges facing the health care industry, ideas from other industry sectors, competing organizations, and different generations of leaders must be sought out and considered. We hope that the conversations and ideas expressed in this journal contribute to that effort.

The WHLE Editorial Staff

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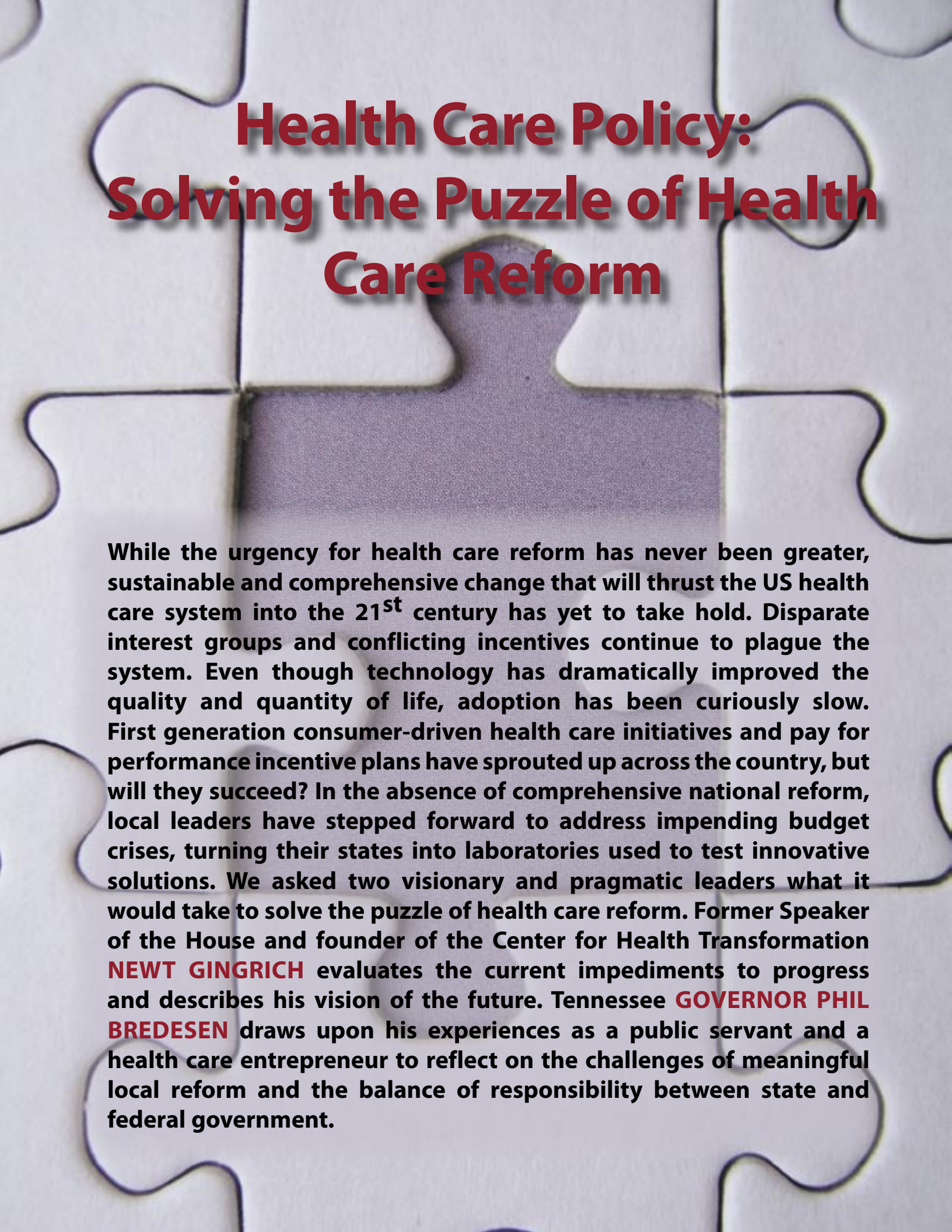
TABLE OF CONTENTS

Health Care Policy: Solving the Puzzle of Health Care Reform



While the urgency for health care reform has never been greater, sustainable and comprehensive change that will thrust the US health care system into the 21st century has yet to take hold. Disparate interest groups and conflicting incentives continue to plague the system. Even though technology has dramatically improved the quality and quantity of life, adoption has been curiously slow. First generation consumer-driven health care initiatives and pay for performance incentive plans have sprouted up across the country, but will they succeed? In the absence of comprehensive national reform, local leaders have stepped forward to address impending budget crises, turning their states into laboratories used to test innovative solutions. We asked two visionary and pragmatic leaders what it would take to solve the puzzle of health care reform. Former Speaker of the House and founder of the Center for Health Transformation NEWT GINGRICH evaluates the current impediments to progress and describes his vision of the future. Tennessee GOVERNOR PHIL BREDESEN draws upon his experiences as a public servant and a health care entrepreneur to reflect on the challenges of meaningful local reform and the balance of responsibility between state and federal government.

Into the 21st Century of Health Care

Since retiring from Congress in 1999, former Speaker of the House **NEWT GINGRICH** has devoted much of his time to the transformation of health and health care. In 2003 he authored the book Saving Lives and Saving Money and founded the Center for Health Transformation (www.healthtransformation.net), a collaboration of public and private sector leaders dedicated to creating a 21st Century Intelligent Health System.

During his twenty years in Congress, Speaker Gingrich was committed to improving America's health care system, co-chairing the Republican Task Force on Health for four years prior to becoming Speaker. Under his leadership as Speaker, Medicare was improved, investment in medical research was dramatically increased, and FDA reform was enacted to allow for quicker approval of and access to new medicines.

Mr. Gingrich is currently a member of the Advisory Board for the Agency for Healthcare Quality and Research and sits on the Board of Regents at the National Library of Medicine. In addition, he co-chairs the National Commission for Quality Long-Term Care. He has received numerous honors and awards related to his work in health transformation, including the 2005 HIMMS Advocacy Award for his leadership in advancing information and management systems for the betterment of human health.

Here, Mr. Gingrich shares what inspired his shift to health care, his opinion on the 1990s reform movement and what could be right about health in the 21st century.

WHLE: You left office in 1999 and by 2003 you wrote Saving Lives and Saving Money and founded the Center for Health Transformation. What inspired your shift to health care?

NG: When I stepped down as Speaker in January of 1999, I decided that I wanted to go back and reinvest in science and technology and build up my own intellectual understanding, so I spent the better part of the year with Georgia Tech, MIT, National Science Foundation and others. I decided that I would focus on two areas: national security and health. They are both life and death, they are both complicated, they are both big. Health is bigger and more complicated. Health is about 30 times more complex than national security! We worked from 1999 to about 2002 trying to understand not what was wrong with health, but where health could go and what could be right with health. We began to develop a model that we outlined in Saving Lives and Saving Money. We wrote that book in part for the Bush administration and the House and Senate Republicans to outline 'here's what the right policies could be.' It's a non-partisan book - I have worked with Democrats such as Hillary Clinton and Patrick Kennedy - it was written and designed to say 'here's where we ought to go.'

After we wrote that and we kept talking with people for another year, I concluded that when you have a system the size of the health system, 16% of the economy, you can't march it into the future. You'll never have the energy to get it organized into a march, but you can migrate it. If you think about bees swarming, you can get an energy level moving in the right general direction. You encourage this hospital to do the right thing and that company and this governor and that state legislator, and gradually over time you can have a migration to a much higher-value system, which we call a 21st Century Intelligent Health System.

WHLE: And what defines your vision of a 21st Century Intelligent Health System?

NG: There are three very simple principles. First, everything is centered on the individual, so they become the center of knowledge, the center of choice, the center of responsibility, the center of decision-making.

Second, everything moves to prevention, wellness and early detection, with acute care as the last step, not the first step. And finally, everything is brought together by information systems. We estimate that the world of scientific knowledge is accelerating between four and seven times the rate of the last quarter century. We think, literally, somewhere between four and seven times as much knowledge will be generated in the next quarter century of your life. If that's true, then what you need is a 21st Century Intelligent Health System so that the right new scientific knowledge is reaching you when you need it, and you are able to find the right doctor who is also attached to the right knowledge. You can't do it with paper.

"Health is about 30 times more complex than national security!"

WHLE: The benefits of technology are obvious, yet adoption has been painfully slow. Why is that so?

NG: It's painfully slow because the payors are all stunningly short-sighted. This is a transaction-based system. Medicare is a stunningly dumb way to purchase health care because it is all transactions. I have tried for three years to convince the administration that going to an electronic system will save them money. Now, Fedex knows it will, UPS knows it will, Bank of America knows it will, American Express knows it will, but somehow we can't get the Congressional Budget Office and the Office of National Budgets to understand the 21st century. These are people who keep coming back and saying stage coaches are cheaper than airplanes. Why would you want to have an airplane?

WHLE: So what is the key to stimulating adoption of technology?

NG: You win the argument. Gradually, you are seeing us win it and you are seeing a steady migration. Florida now has a website where you can go on-line for a particular drug and it shows you every pharmacy in the area and the price. In one particular neighborhood the difference in price is a factor of seven. Now that is not going to last very long! They also have a website that shows you quality outcomes of hospitals, and that begins to change things. It is the very first state to really adopt a 21st century model for information.

So you will see more and more of this. Sutter Health and HCA, which are two of the biggest hospital systems, are both now electronic. Kaiser Permanente is now electronic. You are seeing the migration. The Jacksonville Mayo Clinic has been electronic since 1996. I was recently having dinner with two of the largest insurance companies in the United States. Both of them now have crossed the watershed; both of them are moving towards electronic systems.

WHLE: Technology is a double-edged sword. On one hand it has improved the quality and quantity of life, but some analysts have referenced it as a key driver of costs. For example, patients want and often receive the latest technology independent of cost.

NG: I believe that confuses the symptom with the problem. If you had a third party payment automobile system, the number of people who would need Ferraris would explode because if it is free, why not buy it? So you have a system where there is no effective reference for me in terms of what I have in the game. You walk in and say an X-ray would probably be alright, but we could give you the newest and most fabulous PET scan. Then, the doctor decides to go get a PET scan instead of an X-ray because, after all, shouldn't you have the very best?

Let me give you the other side of that. Every time I go the dentist's office, I get an X-ray. Do you notice it is not given by the radiologist? It is given by the dental technician. Notice it is cheap. No one has done a study of comparative economics in dentistry where people tend to pay on their own. Same thing is true in cosmetic surgery, which is almost all non-third party payment. It has actually risen below the rate of inflation for ten years. It is cheaper today in constant dollars than it was ten years ago because you have had competitive delivery. LASIK surgery is the same. It is generally paid for by the person who gets it. LASIK surgery has collapsed in cost.

I am not very impressed with academics who inherently believe in the bureaucratic control model and refuse to analyze why prices go up and then decide that somehow we need a new control over technology on top of the controls we already have.

WHLE: You mentioned the importance of individual responsibility and consumer empowerment. With increasingly alarming statistics on obesity and the incidence of childhood diabetes, do you really believe that the average American is capable of effectively managing his or her health?

NG: Not always. We have to have a whole new series of social inventions. Quarantine was a social

invention; it began when we began to understand that germs were spread by individuals who are vectors of disease. We need new social inventions. Remember, if you think about all of American culture - this is the freest society on the planet - the number of Americans who are genuinely dysfunctional is significant. Now, it is a very small number of total society. We have 300 million people. If 3% of our society is dysfunctional, it's 9 million people. That 3% may be drug-addicted, they may have genetic disadvantages, they may have been unlucky at birth, they may have been born into a neighborhood where nobody works. We don't have today a strategy for reintegrating people who are currently dysfunctional. That's a very profound and very important question.

If you want to see an interesting example of this, go back and look at the Rockefeller Foundation's activities in the South for things like hookworm and ringworm, teaching people how to wash their hands, convincing them that they had to use toilet paper. The period of the 1890s to the 1930s was one of the great periods of public health because agrarian people were learning the habits of urban living and there was a conscious learned cycle.

WHLE: Moving past the individual, what are the implications for employers?

NG: I would like to see the tax code rewritten so that there is the same tax advantage whether you buy your own insurance or the company buys it for you. I don't see any great advantage or disadvantage to the company buying your health insurance, but there may in the long run be some advantage to buying your own insurance and keeping it for your lifetime. And I don't like the idea that people are trapped in employment by their need for health insurance. We are working on a model here at the Center for 100% insurability, where the whole country is insured. Now this is not the same as a single payor model; we want a 300 million payor model.

WHLE: Understanding the perspective of various stakeholders in the health care reform debate is important. Many analysts attribute the failure of the 1990s movement for health care reform to the lack of alignment among key stakeholders and interest groups, consumers, payors, employers and physicians, just to name a few. Where are we on bridging the interests here?

NG: Well, I would argue that the 1990s movement failed because it was a nutty proposal. The idea that you are going to build a government-controlled, centralized system immediately after the fall of the Soviet Union had to be one of the great moments of not understanding where the world is going. The world is going towards more personal responsibility, more personal opportunity, use of massive databases that allow you to live a life where your credit card works everywhere on the planet, and an ability to organize information totally outside of bureaucratic control models. The 1990s movement was the last great stand of a European style control model - at least I hope it was the last stand! I hope that we continue to move beyond that to a world where you get a defined contribution, you know where you stand in line, and if you are sufficiently poor we give you a tax credit or a voucher to help you out. We understand upfront what we are doing. It is very clean, very simple, and you are responsible for making your own decisions.

"I think you ask the core question every morning 'What is in the best interests of the health of the average American?' and you let the stakeholders reorganize themselves around the answer. Don't try and deal with the stakeholders."

WHLE: And what about the alignment of stakeholders? Is agreement on comprehensive change possible?

NG: I think you ask the core question every morning, 'What is in the best interests of the health of the average American?' and you let the stakeholders reorganize themselves around the answer. Don't try and deal with the stakeholders. Nobody got up in 1890 and said, 'Gee, I wonder what we should do about transportation? Let's go ask the stagecoach owners!' They got up and said, 'I think I want to invent the airplane,' that's the Wright brothers in Dayton, 'I think I will mass produce cars,' said Henry Ford in Detroit, and they just went out and did it. They were trying to optimize the range of choice you have as a citizen for transportation. So I would say the same thing now: focus on what would give the average citizen the longest possible life with the highest quality of life with the lowest cost. And then tell all the stakeholders, 'Reorganize yourselves around it.'

I used to represent the Atlanta airport during airline deregulation. Deregulation combined with open entry to markets combined with Travelocity and Expedia and e-ticketing led to the following price patterns: twenty-three cents per passenger mile in 1978 dropping to twelve cents per passenger mile in 2003 in constant dollars. And, Southwest Airlines became the largest domestic carrier.

Now, you take any state Medicaid budget or take the Medicare budget. If you could apply that kind of a price pattern, you just blew apart every budget projection for the next generation. Aviation in 1978 was considered 'complicated.' Nobody went to Delta, United, and Panam and said 'Gee, would you redesign this?' They said, 'What if we went to a really free market, with open entry for competitors?' You suddenly got more choices to fly more places in the world.

So why shouldn't health care be the same way? It's a totally different way. All these public policy wonks keep trying to find some bureaucratic, mediated control model when all around them we see the modern world turning; it's just not emerging in government. Take a look at *21st Century Entrepreneurial Public Management*, which is a paper I have written on the scale of change we need to have in moving from the obsolete bureaucratic public administration model we inherited to a system compatible with Fedex, UPS and Google.

That's why I want to move the decision back to you. If you keep the decision in the national capitol and state capitol, interest groups can organize and protect themselves. If you create new systems where you are beginning to make the choices, interest groups can't protect themselves. No local store would have voluntarily approved Walmart. No major airline ever voluntarily approved deregulation. So my goal is to communicate a message to the average American where the average American says to the elected official, 'I want to know cost and quality before I choose, I want it on-line, and I am willing to have some responsibility, but I want real insurance if I get really sick.'

WHLE: Let's shift to the responsibility at the state level and flurry of activity around Medicaid reform. Is Medicaid a viable model in the future?

NG: We think you need to completely replace the Medicaid system with a 21st Century Responsible Citizen's Medicaid Act. We break the system into three components. First, the capabilities component for people who are born with disabilities and who want to use modern technologies in order to try to build the capabilities to maximize their ability to pursue happiness. Second, a relatively healthy younger person's system which really is a voucher that can be used to buy health insurance. That's for people who are currently in the Medicaid pool who are relatively poor, but who are actually pretty healthy. And third, there's the challenge of active, healthy aging and quality long term care for people, and that's where I am co-chairing a commission with Senator Bob Kerrey to look at fairly major breakthroughs. We think there ought to be three totally different programs, three totally different structures.

And one of the things we're working on is the idea of citizen responsibility, and the notion that everyone should pay something, even if it is only twenty-five cents. You want to get people into a rhythm of participating, of being responsible, of being involved, and having some sense of what they are making decisions about. We think when you teach people irresponsibility, you actually weaken their decision capabilities and you weaken the quality of their life.

WHLE: You have said before that entrepreneurship is a vital part of health care transformation; a whole section of Saving Lives and Saving Money is dedicated to health care entrepreneurship. Do you have any advice for our readers who are aspiring entrepreneurs?

NG: Read two books: Clayton Christiansen's The Innovator's Dilemma and Peter Drucker's The Effective Executive. And we have a brand new book that will be out this spring called The Art of Transformation that Nancy Desmond (CEO of the Center for Health Transformation) and I are writing. I always say the following words to young people: dream big, work hard, learn everyday, enjoy life and be true to yourself. You have to have the courage to hear 'No' and you cannot allow the 'No's' to kill you. So part of my advice to young people is, if you want to be an entrepreneur, remember that the Wright brothers used to take enough extra wood with them from Dayton down to Kitty Hawk so that they could keep rebuilding the plane, because they wrecked it five or six times a day. Real entrepreneurs make lots of mistakes, but if you persevere, you learn a lot from the mistakes and one day you'll succeed. And then people will decide that you were lucky! ■

Special Thanks to Megan H. Meehan, Press Coordinator, Center for Health Transformation

Taming TennCare

PHIL BREDESEN, the 48th governor of Tennessee, took office January 18, 2003. During his first three years in office, Bredesen brought a new level of candor, openness and accountability to state government with a promise to "focus energy on real results by leaving behind predictable and stale political debates." Most importantly, Bredesen took control of TennCare - the state's financially troubled Medicaid-expansion program - by preserving full enrollment for children and pursuing innovative initiatives such as making better use of health information technology. Even after necessary reductions in adult enrollment to maintain TennCare's fiscal balance, the program remains one of the most generous and comprehensive state health care plans in the nation.

Before serving as Tennessee's governor, Bredesen built a reputation for effective leadership as the mayor of Nashville from 1991 to 1999. Prior to entering public service, Bredesen earned a bachelor's degree in physics from Harvard University and was a successful health care entrepreneur. Between research trips to the public library, he drafted a business plan at the kitchen table of his apartment that led to the creation in 1980 of HealthAmerica Corp., a Nashville-based health care management company that eventually grew to more than 6,000 employees and traded on the New York Stock Exchange. He sold the company in 1986.

Here, Governor Bredesen evaluates the success of his Medicaid reform strategy. The US government's reliance on Medicare and Medicaid, he says, is like riding a creaky, ancient horse. His advice? Stop messing around at the edges and address the structural issues if you want to be successful.

WHLE: You were one of the first governors to take on Medicaid (TennCare) in your state. What was the climate like in 2003 when you entered office, and how did you craft your TennCare reform and roll-out strategy?

PB: TennCare was unique in its breadth and its comprehensiveness. Tennessee had the highest proportion of citizens on Medicaid compared to any state in the country. We spent the highest proportion of our state's budget on Medicaid compared to any state in the country. Other states are not as far advanced in their reform efforts because they don't have a program quite as comprehensive as Tennessee had in 2003.

I looked at TennCare reform as a process that required a lot of careful thought, and not just what is the 'reform du jour.' We went out and hired a consulting company, McKinsey, to come in and take a broad look at our program with two questions in mind. First, is TennCare viable in something like its current form moving forward? Second, if it is not, what is the menu of options that we might look at to bring it more under control? We funded them privately because it seemed like the appropriate thing to do.

They came back and basically answered those questions for us. First, it's not viable in its current form. Over the next five years, it would consume between 80% and 90% of all new dollars that we raise in tax revenue in the state of Tennessee - obviously completely unacceptable. TennCare would become the gorilla that comes to the table and eats all it wants, and if there are any crumbs left over for education, then we get to fight over them. Second, they pointed out some areas where we could trim the very comprehensive set of benefits to retain the important things, let some of the other things go, and thereby save money.

Tennessee had entered into some consent decrees with a public interest law firm, the Tennessee Justice Center, that sued the state. We needed their approval to do this benefit trimming and they wouldn't give it to us, so we were forced to take an alternative route.

Some benefit trimming we could do, and we actually started removing some people from the TennCare roles. That has now happened and it has gone on, if not totally smoothly, at least without any major problems. We are getting ready to take the next steps; we have disassembled this program into various pieces. Now, how do we put it back together in a way that is more sensible and more maintainable for the long run?

WHLE: You have acknowledged now that you want to address those who were left uninsured (a little over 600,000). What solutions do you see in store for them and how will you sell the solutions to key stakeholders? Is Medicaid the right vehicle for addressing this group of people?

PB: I don't think Medicaid is a very good vehicle for dealing with the uninsured. The benefit package that it has was designed to be for women and children. That set of comprehensive benefits is not particularly appropriate or suitable for large numbers of people in other types of circumstances. What I would like to do is to find a way, and we are working on this actively, to offer to people who are uninsured some sort of insurance. This is not some sort of super comprehensive plan that Medicaid is, one that might be suitable for a woman and her children, but one in which the cost of the plan is shared across several different parties. I think the solution to the way you get a person employed in a small company that doesn't have health insurance is not to argue whether the company pays for it or whether the government pays for it. You get everyone to step up and pitch in and pay some. If we, the state of Tennessee could pay some, if the federal government should pay some, if the individual could pay some, if the company could pay some, you might be able to then craft a plan that would at least meet the basic health needs of a person at a price that was affordable to each of the parties involved.

I don't believe that we will get federal participation to start. I think that is probably a second step. I certainly hope that eventually we can bring them in because we send a lot of tax money to Washington, and I would like to get some of it back for our health care needs. We need some underlying kind of insurance that is underwritten by the federal government that takes care of major problems and major expenses but doesn't attempt to provide first dollar coverage for everything that anybody might need.

WHLE: So what is the appropriate role of federal government?

PB: I think ultimately the federal government has got to recognize that the current Medicaid and Medicare system was designed in 1965. What health care can do has changed dramatically since then. The health care economy bears no relationship to what it was like in 1965, and yet we continue to push forward with extensions and add-ons to that program. The federal government has got to realize that they are riding a very creaky, ancient horse here. They need to devise a much more modern system.

"We are today paying $220 million a year for antihistamines and antacids for people on TennCare, and yet I can't spend a dime on blood pressure medication for people who are uninsured - it's crazy."

I have outlined some of the basic principles that I thought the system ought to be built around. First, everybody ought to have to pay a little something for everything; there has to be some economic tension in the system or the costs are going to continue to spiral out of control. Second, you ought to pay for what is important. We are today paying $220 million a year for antihistamines and antacids for people on TennCare, and yet I can't spend a dime on blood pressure medication for people who are uninsured - it's crazy. Third, pay for what works. Just because a drug company puts a new drug on the market or an equipment company puts a new machine on the market doesn't automatically mean that it is better than something that was there before. We need to move out of being simply payors and turn into intelligent purchasers of health care. We need to make some choice among the things that are effective and reasonable and sensible expenditures of money and which ones are not.

I ultimately believe that the federal government has role to play in providing some underlying kind of universal health care. People ought to have the ability to maintain the basic kind of health care when they move from job to job or become unemployed. We need a national health care policy that is more intelligent and makes better choices about what stuff is really important. If you have appendicitis, nobody doubts it needs to be paid for. On the other hand, if you have a cold, there is not the same moral imperative that you have the latest and greatest antihistamine. Until we differentiate

between the two and give them different priorities, we are always going to have an inefficient system.

WHLE: What role should technology play as states test different initiatives to reduce costs and improve quality of care? Is technology going to cure the cost problem?

PB: I think technology is important. In particular, some way to integrate medical records so that you don't repeat tests and doctors have access to more information than just what is immediately accessible and available. But technology by itself is not going to solve this problem. People love to talk about technology because it is a 'pre' thing - nobody objects to putting technology in place. The only way that you are ultimately going to control costs is if you have to have the ability to say 'No' once in a while. You have to say to someone, 'I know you want to latest antihistamine here, and it is $3 a pill. No, we are not going to pay for that.' Until you are willing to do that, you are never going to solve this problem. There is certainly a huge role for technology in health care, but anyone who thinks that it is the solution to the economic problem of the industry is not right.

"But technology by itself is not going to solve this problem."

When I talk about the cost of health care, I look at it in a very practical way. I think we need to cover 45 million Americans who don't have health insurance with at least something. We now spend over 15% of our GDP on health care, and yet we still have 45 million people who are uninsured. It seems unlikely to me that we are going to solve the problem by simply stepping up to the additional costs driving that 15%-16% of GDP. You have got to find some way to wring some of these inefficiencies out of the system and reinvest the money and bring more people on to the system. That is the core of what we are doing in TennCare.

WHLE: Let's switch to some of your experiences before your days as a public servant. You started off your career in health care and then as a health care entrepreneur. Can you tell us more about that?

PB: I have worked in the health care industry for much of my adult life. I started out working for an equipment subsidiary of G.D. Searle & Co. When I came to Nashville, I was in the hospital industry for a brief time with one of the proprietary hospital companies. In 1980 I started my own company, which was one of the early HMO management companies. The company we had was primarily a closed panel company, or staff model HMO. I grew that up from my house to a good-sized public company, a New York Stock Exchange, 6,000 employee company. While my experience is 15 years out of date, I learned an awful lot about how health care really works and how the delivery systems really work and that has been an enormous help to me in trying to sort my way through the issues with Medicaid and health care here in our state.

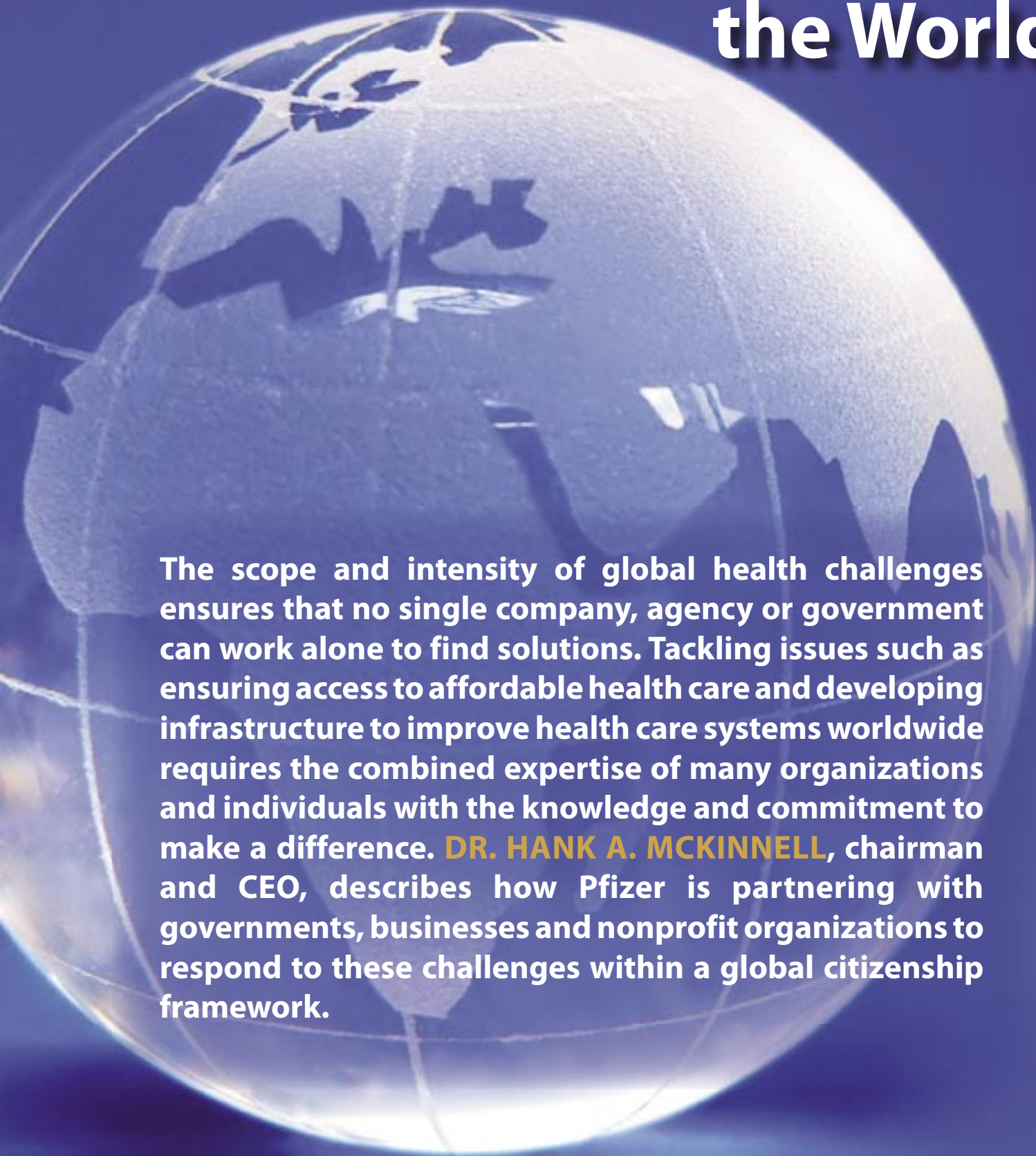
WHLE: What is your advice to governors and state leaders taking on Medicaid reform? What about to entrepreneurs entering the health care industry?

PB: My advice to governors is that this problem is a fundamental, structural problem. You can't solve it by messing around at the edges. It is a much bigger problem that you can't solve by just adding technology here, or some checking here, and a drug smart card here. There are some fundamental structural problems with Medicaid, and if you don't tackle those, you won't be successful.

I think health care is a great field in which to be an entrepreneur. Health care is going to keep growing as a proportion of the economy for the rest of our lives. But I think the entrepreneurial world has gotten a little skewed by a reimbursement mechanism which can't be sustained over the long run. Health care entrepreneurs need to be looking down the line to a time when cost-effectiveness plays a much bigger role in the decisions that are made in health care. They need to concentrate their energies on trying to improve the cost and the quality of the services, just like they do in virtually every other field in which entrepreneurs operate. ■

Special Thanks to Lydia Lenker, Press Secretary, Governor of Tennessee's Communications Office

Global Health: Partnering to Improve Health around the World



The scope and intensity of global health challenges ensures that no single company, agency or government can work alone to find solutions. Tackling issues such as ensuring access to affordable health care and developing infrastructure to improve health care systems worldwide requires the combined expertise of many organizations and individuals with the knowledge and commitment to make a difference. DR. HANK A. MCKINNELL, chairman and CEO, describes how Pfizer is partnering with governments, businesses and nonprofit organizations to respond to these challenges within a global citizenship framework.

A TOTAL FRAMEWORK FOR CORPORATE CITIZENSHIP

HANK A. MCKINNELL, PHD, is the twelfth leader of Pfizer, Inc., the world's largest research-based pharmaceutical company, in its 157-year history. He joined Pfizer Japan in 1971 and his career includes service as president of Pfizer Asia, Pfizer, Inc. CFO and COO, and president of Pfizer's Global Pharmaceuticals Group, which he drove from number 14 in its industry segment in 1992 to number one in 2001, the year he was elected chairman and CEO. He is the chairman of the Business Roundtable and the Stanford University Graduate School of Business Advisory Council. He is a fellow of the New York Academy of Medicine and a Trustee for the New York City Public Library. Dr. McKinnell holds a bachelor's degree in business from the University of British Columbia, and MBA and PhD degrees from the Stanford University Graduate School of Business. He is the author of A Call to Action: Taking Back Healthcare for Future Generations, published by McGraw-Hill in 2005.

Here, Dr. McKinnell describes Pfizer's commitment to improving health worldwide. He discusses Pfizer's efforts to partner with stakeholders in government, public health, policy, education and NGOs to develop innovative solutions to transform health care. Dr. McKinnell stresses the importance of corporate citizenship as the key to defining an organization's role and impact in local and global communities, and to improving business performance.

Last year, a Pfizer scientist, Jennifer Brown, wrote to me from a refugee camp in Northern Kenya, where she was hard at work computerizing the records of a makeshift hospital. In a region where one baby in 20 is born with HIV, she described how she had to transcribe entries from handwritten script.

"I keep typing the word 'die'," she wrote, in words so poignant they need no further elaboration.

Jennifer worked with the International Rescue Committee as a member of a relatively new Pfizer program called Global Health Fellows. Twice a year, we send a handpicked group of medically-trained colleagues to work on the front lines of the battle on HIV/AIDS. The assignments, mostly in Africa, are with nongovernmental organizations (NGOs) and last four to six months. It's a program that transforms its participants, and it is now being hailed by others as an example of corporate social responsibility.

While we at Pfizer greatly appreciate the good words, I sometimes get concerned that people view programs like Global Health Fellows as somehow separate from all the other activities we pursue. I always point out that all we do, in every aspect of our business, falls under the umbrella of "responsible." First and foremost, we spend every working day trying to help people live longer, happier, healthier lives. Our work, in my view, is among the most responsible lines of work you can imagine. While we are certainly proud of programs like Global Health Fellows, and of our status as the world's most philanthropic company, we see these activities in terms of an overall framework of corporate citizenship. Our job, in whatever we do, is to listen and respond to the needs of a long list of people and groups who have a stake in our business. This list starts with patients, but it extends to customers, colleagues, investors, business partners, governments, NGOs, and the local communities in which we live and work. Listening and responding to these stakeholders is simply indispensable in today's world. Our company operates in well over 150 countries. Our products affect the lives of hundreds of millions of people. We simply cannot afford to behave as though our operations have no real impact beyond our shareholders. We understand that in many nations, a company the size of Pfizer is a major presence, and even seemingly small actions can have enormous effects.

This reality was driven home to me by an experience I had as Pfizer's country manager in Iran, during the years immediately preceding the revolution in the late 1970s. When I first arrived at Pfizer's facility in Tehran, I noticed a knot of young men standing around outside the entrance. When I asked why they were there, I was told that these were day laborers, hoping to get hired for some shift work. The lucky ones earned a few bucks. The others went home disappointed, and, I'm sure, angry. Even though other executives assured me that "this was how things were done" and that there was nothing unusual about having a pool of ready laborers hanging outside our gates, that reality just didn't sit right with me. There had to be a better way to interact with these workers, even though we couldn't hire them all. I put this one on my "to do" list.

"Our products affect the lives of hundreds of millions of people. We simply cannot afford to behave as though our operations have no real impact beyond our shareholders."

It took several years, but ultimately, we did improve conditions for the day laborers. Instead of expecting them to come to our gates for work, we sent a bus every day to a designated spot in downtown Tehran to pick up the people we needed. Their pay was substantially raised, and they ate for lunch the same fare that was served to me and all other plant workers. At the end of their shift, the bus transported them back downtown, closer to their homes. I'm sure that more than a few Pfizer people thought I was being excessively solicitous, but I never thought that treating people decently was anything for which to apologize. Maybe helping improve the lot of a small number of day workers wasn't much in the grand scheme of life. Our good intentions certainly did nothing to divert the sweep of events that soon engulfed Iran. But everything worth doing starts with

Global Health Fellow Deb Wafer in Eastern Uganda working with the Foundation for Development of Needy Communities

Global Health Fellow Lisa Gesierich spent her time at the Family Health International, Regional Economic Services Office (REDSO) in Nairobi, Kenya, developing project briefs, press releases and case studies, as well as assisting with developing a communication strategy and dissemination plan for these materials.

the efforts of a few committed people. I like to think that our efforts helped these laborers put a little more of themselves into their work, and perhaps, to think a little better of our company and all Americans.

This story makes a simple point about citizenship. A citizen is not merely an inhabitant of a particular place or nation, but is also a truly involved participant possessing rights, responsibilities and duties. Citizens, in the real sense of that term, can't be purely self-regarding. More is expected - including a caring spirit when it comes to neighbors and neighborhood, and a willingness to become involved in nation and world. To be a citizen is to focus on making a real difference to those in your community. To be a corporate citizen is to center on helping not just community, but the larger world. In our 157-year history, Pfizer has always sought both to do well and do good. We have a strong foundation of well-defined corporate ethics, a notable record of philanthropy, and a commitment to engage colleagues in our purpose and work. We have long been recognized as a good employer and as a generous company.

"No one company, agency or government can solve such a longstanding problem on its own."

However, as we entered the 21st century, we found that our framework for "doing good and doing well" had to change. The global research-based pharmaceutical industry is one of the world's most complex - and controversial. It is also a high-risk industry, where research successes are rare. More than a billion dollars is risked on every new medicine. Only three out of ten medicines that are approved for use ever recover their research and development costs. But such research is essential, both for patients now, and for patients with unmet medical needs. With more than 90 percent of all new medicines coming from companies like Pfizer, society must find ways to not only get patients access to new medicines, but also to ensure the right rewards for companies that continue to innovate. Societies understandably expect more from research-based pharmaceutical companies than from companies in other industries, mainly because our products greatly affect the length and quality of life. In addition, Pfizer went from a solid multinational to a dynamic global company in just 15 years, and is now the world's most recognized pharmaceutical brand. As the

saying goes, "people expect more from a leader."

So, given the vast complexity and increased scrutiny of our business, Pfizer has had to put into place a framework for global citizenship that is both relevant everywhere and sustainable over time. This global citizenship framework defines how we engage stakeholders and conduct business responsibly throughout the world. It is a comprehensive set of values, policies, practices, and programs, which are integrated into our business operations worldwide. We recognize that in today's marketplace, a pharmaceutical company must have a total ethical framework in order to compete.

Our priority is simply stated - keep people healthy in cost-effective ways. As a first "layer" in achieving that priority, we understand that we have company-wide responsibilities, not vastly different from those of other global, publicly held companies. These include practicing good governance, ensuring legal compliance, adhering to our corporate ethics, respecting our colleagues, protecting the environment and supporting the communities where we live and work. While there can be legitimate differences of opinion in what constitutes "best practices," Pfizer has a heritage of doing the right thing.

The second "layer" of the framework, and a distinguishing factor for Pfizer, demands evolving approaches to corporate responsibility for each of our business operations. These largely center on greater transparency. In the past five years, we've joined Transparency International, a group committed to eliminating bribery and corruption. We have also become a partner in the UN Global Compact, endorsing a shared set of principles on human rights, labor, environment and ethical behavior. In addition, in this age of the Internet, we understand the demand to have public access to the results of late-stage clinical trial data. We have already posted data from hundreds of studies. We are also disclosing them in summary, and working with the WHO and others to create trial registries. Our outreach to patients is also being guided by stronger commitments to discussing risks versus benefits and alternatives to our medicines.

Perhaps the most difficult area is doing more to ensure that more people get better access to the medicines they need. Our vision is a society where medicines are available regardless of limits of income. This is a shared goal and responsibility with society at large. We are taking critical steps, including ensuring that all Americans, with or without insurance, can afford

Global Health Fellow Trish Hurley in Eastern Uganda working with the Foundation for Development of Needy Communities

our products; negotiating global agreements to help poor nations get medicines far more cheaply; and building a medical infrastructure in developing nations. We are performing concrete actions to help improve health care systems worldwide, while still working within the reality that no one company, agency or government can solve such a longstanding problem on its own. Together, as partners, we can make real progress, such as the International Trachoma Initiative where there is now real hope of eliminating blinding trachoma in 15 years.

The final "layer" of our corporate citizen framework is to use our vast knowledge and unmatched global scale to develop innovative approaches to improving health. Pfizer's contribution in this sphere is our Global Health Fellows Initiative. Jennifer Brown and her fellow Global Health Fellows represent one Pfizer example. We are also examining how we can more effectively put our knowledge of both disease and wellness to use by investing in conquering the diseases of the developing nations, such as malaria, by pioneering new approaches to employee health care and prevention.

Overall, our view is that corporate citizenship is no different than any other long-term corporate investment. Our commitment makes a strong statement about what Pfizer means by our mission to be "most valued." A strong framework for corporate citizenship helps us build relationships with stakeholders, which in

turn helps improve our external operating environment, which improves our business performance, and raises the bar for our competitors. We can't discover the next breakthrough medication if we lose the trust of the people who buy our products or work with us.

That's why, for the first time in our company's history, Pfizer's first-quarter 2003 business performance report included more than financial results. It also described our efforts to expand access to medicine and demonstrate good corporate citizenship. We want to be judged by our business results, by how we work in partnership to increase access to medicines for patients today and tomorrow, and by our commitment to corporate citizenship.

Like all human organizations, Pfizer is far from perfect. We grapple with legitimate differences of opinion on the roles of public companies in our global village. We believe that market forces are often the most effective in securing the most good for the most people. We see that medicine in general and pharmaceuticals in particular are lightning rods for controversy. Our goal is to replace what was often a piecemeal, programmatic approach to corporate social responsibility with a far stronger, more integrated, and more global platform influencing all we now do and every decision we make.

Easy? Not a chance. But rewarding? Ask Jennifer Brown, and the people she's helping to save. ■

"We can't discover the next breakthrough medication if we lose the trust of the people who buy our products or work with us."

Personalized Medicine: The Road Ahead

Personalized medicine has often been described as one of the new frontiers of health care. However, it is often difficult to identify "personalized medicines" or differentiate the practice of personalized medicine from the standard of care. Despite promises of a revolution in health care, the adoption of personalized medicine has been much more gradual than some have anticipated. We spoke with four leaders in the field of personalized medicine to illuminate all sides of this debate. Wharton alumnus **DR. STAN BERNARD** lays out the landscape of personalized medicine and provides a roadmap for the executives that will face an industry shaped by personalized medicine technologies. **MARA G. ASPINALL** of Genzyme elaborates on the commercial and social promise of personalized medicine. **DR. LEE E. BABISS** of Roche discusses the scientific challenges that personalized medicine must overcome. **DR. LAWRENCE J. LESKO** of the FDA brings the perspective of a regulatory agency eager to drive the adoption of a set of technologies that may create safer, more effective drugs.

THE BEGINNING OF A NEW ERA IN MEDICINE

STAN BERNARD, MD, MBA, is president of Bernard Associates, a health care and pharmaceutical industry management consulting firm offering strategic planning, marketing, and business development services. Dr. Bernard is a nationally recognized consultant, speaker, and author. He has been featured on national television and in leading publications, including the Wall Street Journal, Business 2.0, and Business Week. He has published over 50 book chapters and articles on health care topics. Previously, Dr. Bernard served as a consulting principal at A.T. Kearney and held several executive positions at Bristol-Myers Squibb. He served as US product manager for the launch of Pravachol, as US Managed Care medical director, and as US director-pharmacoeconomics. Previous positions included those in Worldwide Business Development, US Medical Operations, and US Medical Services. Dr. Bernard received his MBA in marketing and health care management from The Wharton School. He received his MD from Baylor College of Medicine.

Here, Dr. Bernard argues that the use of genetic and related information to personalize medical care is the culmination of medicine's long quest to provide the right treatments to the right patients. Furthermore, he believes that the unavoidable shift towards personalized medicine should be embraced by the pharmaceutical industry and provides a checklist for executives to monitor their own efforts.

WHLE: People mean different things when they use the term 'personalized medicine.' How do you define personalized medicine?

SB: Personalized medicine is the use of a person's genetic and related information to help understand and manage disease susceptibility, diagnosis, and treatment. Other terms people use to describe personalized medicine and related technologies include 'targeted therapy,' 'individualized medicine,' 'pharmacogenomics,' and 'pharmacogenetics.' The important distinction is that personalized medicine is not limited to personalized medicine*s*; it signifies a broader definition that includes personal disease risk and detection as well as tailored, individualized treatment.

WHLE: So it is not just about drugs, then, and it is not just about diagnostics. How do you differentiate the various components of personalized medicine?

SB: Personalized medicine is a new clinical approach that applies genetic and related information across the spectrum of medical care, from disease prevention and detection to therapeutic management and monitoring. I classify personalized medicine into two major categories: disease applications and drug (or therapeutic) applications. Among the disease applications, there are two major types: *disease susceptibility* applications and *disease diagnostic* applications. Disease susceptibility applications help determine the likelihood of a person getting a disease. For example, Myriad Genetics' BRCA1/BRCA2 test helps determine the likelihood of a woman getting breast cancer or ovarian cancer. Disease diagnostic applications help to establish or confirm the diagnosis of a disease or condition. For instance, TM Bioscience recently received FDA approval for a genetic test to help diagnose cystic fibrosis.

There are two types of therapeutic applications: *designer* or *targeted drugs* and *pharmacogenetic* or *drug response* tests. These tests help identify how individuals will respond to drugs from an efficacy and safety standpoint. The classic example of a drug response test is HercepTest, a genetic test to predict

the response of women with breast cancer to the cancer drug Herceptin. We have several other examples of drug response applications. Most recently, Roche Diagnostics received FDA approval for its AmpliChip CYP450 test which helps determine patient response to about 25% of marketed drugs.

WHLE: Within drug response tests, two types of tests have received a lot of attention: safety response tests and efficacy response tests. Is one or the other likely to have a more pronounced impact on medicine?

SB: While I am primarily a business consultant, I am also a physician. From a medical perspective, there is no greater initial need than for safety response testing, especially considering that we have over two million severe adverse drug reactions a year causing over 100,000 deaths. A significant portion of these are related to genetic factors. I am very excited about the potential of safety response tests to reduce that death toll.

Two recent cases highlight this issue. GlaxoSmithKline's Ziagen is an AIDS drug that causes a potentially fatal hypersensitivity reaction in about 5% of patients with certain genetic variations. The FDA has been working with GSK to create a test to screen patients needing that particular drug. Similarly, researchers at St. Jude's Hospital in Memphis have developed a TPMT pharmacogenetic test which helps keep Purinethol and related chemotherapeutic agents on the market. Children with cancers treated by those agents take the TPMT Test to identify the 1-2% of individuals who might develop a life-threatening adverse drug reaction because of their genetic profile. Therefore, we have shown that there is the potential, in selected cases, for some drugs to be rescued by the development and use of safety response tests. By preventing those most likely to suffer adverse reactions from taking a medication in the first place, we can adjust our safety predictions for others not at increased genetic risk, thus seeing not only an enhanced safety profile of various medications but also presumably enhanced efficacy as well.

As important as safety is, I believe we are more likely to see some of the efficacy response tests commercialized first, particularly in the area of cancer. There are already some early efficacy tests available for a few cancer drugs, like Herceptin and Tarceva. However, we have also seen that some efficacy response tests, like the one for the cancer drug Iressa, may not be as accurate and predictive of response as we had initially hoped. It is important to recognize that in many cases, genetic testing will not provide black and white answers: there will be many gray areas where we must consider probabilities, not certainties.

WHLE: Popular opinion is that personalized medicine is very futuristic, but you have cited a number of examples of its use in current medical care. How is it that personalized medicine is available now?

"Since Hippocrates' time over 2000 years ago, health care practitioners have tried to personalize medicine."

SB: The most important thing people need to know is that the era of personalized medicine has been underway for nearly two decades. It is already being used by health care professionals to benefit patients today. Let me put this in context. Since Hippocrates' time over 2000 years ago, health care practitioners have tried to personalize medicine without the information or tools to achieve the level of personalization we desire. As we now define it, personalized medicine allows us to enter the newest frontier of medical understanding: the genetic level. Genetic medicine is the ultimate personalized level of intervention because no two human beings have and express genes exactly the same way. If we can manage and treat patients at the genetic level, that is as personal as it can get. We have already begun these sorts of genetic interventions, but the next 10 years will see an exponential increase in the personalized medicine tools in the proverbial black bag.

WHLE: What is the vision of personalized medicine? What value does personalized medicine provide and are we certain of that value?

SB: The vision of personalized medicine is three-fold: to leverage genetic information and applications to better prevent and detect diseases; to develop and tailor treatments for certain diseases and individuals; and to maximize safety and efficacy of treatment options for the individual. Clinically, personalized medicine represents the next era in medicine, the hallmark of the next new frontier in scientific discovery and clinical application. These new genetic technologies have the potential to help health care professionals prevent disease, improve

diagnoses, and enhance safe and effective treatments, all of which will ultimately result in better patient outcomes at a lower cost. Consequently, individual patients will be the primary beneficiaries of personalized medicine approaches, but businesses will benefit as well.

Many business executives still need convincing that personalized medicine is to their advantage and that they need to address this area now. Many executives have been reluctant to dedicate sufficient resources to personalized medicine, pharmacogenomic research, and related activities because of a misconception that personalized medicine will fragment markets and niche their products, ultimately reducing pharmaceutical sales and destroying the 'blockbuster model.' This is a myth. In fact, personalized medicine applications, including both disease and drug applications, have the potential to increase or decrease product shares and market sizes, depending on a host of important factors.

WHLE: In what ways might personalized medicine affect pharmaceutical business models?

SB: Many pharmaceutical professionals are not aware that personalized medicine can actually increase market size or share for products in several potential ways: by recruiting patients from other less effective or appropriate competitors; by increasing use in diagnosed but untreated patients; by expanding to genetically similar disease states beyond a drug's primary indication; by encouraging earlier, preventive use of drugs; by enhancing patient compliance; and by obtaining higher reimbursement for safer and more effective drugs. In addition, personalized medicine has the potential to rescue drugs that otherwise might be withdrawn from the market. The FDA agreed to approve Herceptin only with the HercepTest.

I believe that progressive pharmaceutical companies will actually create a few 'megablockbusters' by leveraging personalized medicine technologies. If we can identify drugs that are shown to be extremely safe or effective for certain individuals by pharmacogenetic tests, they could potentially capture a larger portion of the market. Imagine if pharmacogenetic tests on Lipitor demonstrated superior efficacy or safety over its competitors, efficacy in other diseases, or that drug susceptibility tests identified more patients that could benefit from statin therapy. That is actually a possibility.

There are many other myths that I confront in working with pharmaceutical and other business executives. I often hear that 'personalized medicine won't happen for years, so my company doesn't need to worry about it.' Try telling that to the Ziagen marketing team. Try telling that to the Iressa marketing team. On the other side, there are a number of cutting-edge companies, such as Genentech, which are embracing this technology and actively leveraging it. Clearly, personalized medicine is already impacting the pharmaceutical industry - positively and negatively - in selected situations.

WHLE: It seems as if the industry is heading for a tipping point where having a test may be necessary to maintain competitive advantage.

SB: It is clear that personalized medicine and pharmacogenetics will increasingly be used for competitive advantage by companies for their products. For example, a company marketing a late entrant into a therapeutic category may use a pharmacogenetic test to differentiate the product and take a piece of a sizable market. Herceptin did that. Herceptin started with a small slice of the metastatic breast cancer market and has increasingly taken a bigger wedge, driving nearly $1 billion in sales.

"The battleground for pharmaceutical marketers will increasingly move from their products to the pharmacogenetic test that identifies the appropriate use of their products."

In the future, I anticipate that some companies will develop pharmacogenetic tests and encourage doctors to use their test first to see if their drug will work. If their patient responds well to that drug, it will be used ahead of competitive agents. There will be gradually increasing competitive pressure within the pharmaceutical industry to leverage personalized medicine, which will speed the adoption of the technology.

Over time, the battleground for pharmaceutical marketers will increasingly move from their products to the pharmacogenetic test that identifies the appropriate use of their products. Consequently, we are seeing some of the more progressive companies forming relationships with diagnostic testing companies and seeking exclusive licensing agreements for diagnostic tests and processes. Gradually, drug response tests in some therapeutic categories will become the key product differentiator, more important than clinical data, marketing activities,

or sales detailing.

WHLE: Competitive pressure is one way to move this forward, what are some other likely drivers for personalized medicine?

SB: There are a number of other factors that will influence the adoption rate of personalized medicine. Certainly, legal considerations, including product liability and medical malpractice, will be important. Eli Lilly has already been sued by a widower whose husband died taking Prozac. Subsequent information suggested that he was a poor responder to Prozac-like medications based on his genetic profile. The AMA has warned physicians to become more educated about genomics in order to avoid medical malpractice.

Regulations will also influence the rate of adoption of personalized medicine applications. Generally speaking, the FDA and other regulators are very favorably disposed to personalized medicine because these applications could help ensure the safety and efficacy of the drugs they are regulating. In 2005, the FDA issued guidelines encouraging the use of pharmacogenetic and related information in clinical trials.

Reimbursement will be a powerful influencer of personalized medicine. Most payors are concerned that personalized medicine tests will increase their overall costs, and they fear the increased financial burden of new tests and technologies. However, these applications could ultimately limit inappropriate product and service utilization as well as costly consequences of adverse reactions due to inappropriate or ineffective medication choices. Recognizing this, United Healthcare formed a partnership with Interleukin Genetics in 2002 to evaluate genetic testing to help guide the appropriate use of expensive rheumatoid arthritis drugs.

WHLE: In such a complex environment, who is going to be successful?

SB: There are a wide variety of players and categories of players in the personalized medicine arena. It is premature tell who will ultimately succeed, but there are some early leaders. Among providers, the Mayo Clinic has leveraged their database of a local, genetically-homogenous population. Many genetics companies have demonstrated early successes, including Myriad Genetics, deCODE Genetics, and Celera Genomics. Platform developers such as Affymetrix, whose platform was used for Roche's recently approved AmpliChip Test; leading diagnostic companies, including Roche and Abbott; and laboratory companies, particularly LabCorp and Quest, are all well-positioned. IT companies like IBM and imaging companies like GE stand to benefit considerably. Roche, Genentech, and GSK are among the early leaders on the biopharmaceutical side.

As with most new medical technologies, some will succeed but many will fail. Companies most likely to succeed will be those whose executives have the vision and leadership to leverage the technology and develop appropriate business models for their companies. Just as the field of personalized medicine is based on individual variation and individual solutions, the business opportunities, strategies, and solutions need to be based on individual company assessments, business plans, and customized solutions. There is no generalized approach to personalized medicine. Given that, there are several key steps that business executives should take to help ensure success in this field [see Dr. Bernard's "Executive's Checklist" in the box accompanying this article].

"Just as the field of personalized medicine is based on individual variation and individual solutions, the business opportunities, strategies, and solutions need to be based on individual company assessments, business plans, and customized solutions."

WHLE: On a different note, you are a Wharton alumnus. How has your career led you to your current position, consulting to executives on cutting-edge issues like personalized medicine?

SB: As a young boy, I dreamed of becoming a surgeon. This led me to Baylor College of Medicine where I had planned to study general surgery with people like the great heart surgeon Dr. William DeBakey. While there in the early 1980's, I realized that the evolving managed care model would have a major adverse effect on medical practice. So, I decided to transition from clinical medicine to leverage my medical background in the business world.

During my transition, I was fortunate to get advice from a number of leading health care executives. The most influential advice came from Dr. Tommy Frist, Jr., the CEO of Hospital Corporation of America at

EXECUTIVE'S PERSONALIZED MEDICINE CHECKLIST

Corporate Strategy

- Is personalized medicine on your executive agenda, if so, where?
- What are personalized medicine's implications for your industry and company?
- What is the company's strategy for leveraging personalized medicine in drug commercialization?
- How does the company plan to use personalized medicine for and against competitive differentiation?

Intellectual Capital/Organization

- Does your company have personalized medicine intellectual capital and expertise?
- Does the company have the staffing and resources available to support personalized medicine?
- Has it embedded personalized medicine in corporate processes?
- What personalized medicine training is the company providing?

Business Development / Licensing

- Is the company continually monitoring personalized medicine technologies and companies for partnerships and competitive exclusivities?

Marketing

- What are personalized medicine's implications and applications for marketing products in your specific therapeutic area?
- Does personalized medicine help or hurt your efforts to position your products?
- What is your competition doing with personalized medicine to differentiate its products?

Adapted from Bernard, S., "The Five Myths of Pharmacogenomics," Pharmaceutical Executive, October 2003.

that time. He advised me to go get an MBA in health care management, specifically suggesting that I attend what he referred to as 'the best health care management program in the world': The Wharton Health Care MBA Program. I followed his advice and went to Wharton. I began my post-MBA career at Squibb Pharmaceuticals (now Bristol-Myers Squibb) in Worldwide Licensing and Business Development and held several other executive positions within the company during my time there.

In the mid-1990's, I joined A.T. Kearney, a leading global management consulting firm and division of EDS as a principal in their Health Care and Pharmaceutical Consulting Practice. While at A.T. Kearney, I received a number of requests from business executives saying that they wanted to engage me - not a consulting team - to consult for them. Recognizing the business opportunity, I launched Bernard Associates (www.BernardAssociatesLLC.com) in 1999 and created a novel approach to management consulting. I call this 'Executive Consulting.' In this new consulting model, I work directly with business executives and their teams, leading their intra- or interdepartmental teams through the process using my consulting methodologies, facilitation and project management skills, and relevant domain expertise. The internal team then works on the project under my guidance.

There are three major business advantages to the Executive Consulting approach: increased likelihood of project implementation with internal team buy-in, retention of intellectual capital, and dramatically lower costs. I have successfully grown this practice over the past six years and have had the pleasure to work with seven out of the top ten pharmaceutical companies as well as many other health care products companies, including biotech, medical device, diagnostics, and consumer products companies. I have maintained a connection with the Wharton School by teaching in two different courses: the 'Pharmaceutical Management' course starting in 1991 and the 'eHealth' course starting in 1999. I have also had the pleasure of working with several former Wharton students as clients. ■

THE END OF TRIAL AND ERROR

MARA G. ASPINALL, MBA, is president of Genzyme Genetics, the leading nationwide provider of high quality, complex testing services for physicians and their patients, and a business unit of Genzyme Corporation. Under her leadership, Genzyme Genetics has achieved record growth in sales and profits while establishing itself as a leader in prenatal, reproductive and cancer testing. She also served as president of Genzyme Pharmaceuticals. Ms. Aspinall is an active board member of the Dana-Farber Cancer Institute and the Personalized Medicine Coalition, and previously served as chairman of the Board of the American Cancer Society, Massachusetts. Her Masters of Business Administration from Harvard Business School was enriched with the John P. Stevens Prize for leadership, and she was a *magna cum laude* graduate of Tufts University.

Here, she argues that personalized medicine is the inevitable successor to the current practice of trial and error medicine and that personalized medicine holds the key to reducing spiraling health care costs and improving patient outcomes. Moreover, she argues that successful use of personalized medicine may even improve the public perception of the pharmaceutical industry.

WHLE: Genzyme has a unique presence in both diagnostics and therapeutics. Can you discuss how this has led to the company's activities in personalized medicine?

MGA: Genzyme is a company that is built on the premise of meeting unmet medical needs for serious diseases. In the era of personalized medicine this translates into identifying the right patient at the right time and selecting the right drug based upon specific test results. In order to do that, we have always had two areas of focus: diagnostics and therapeutics. Both areas target meeting unmet medical needs in a unique way and are focused on getting physicians what they need to treat the patient.

Genzyme Genetics is one of the original core businesses of Genzyme Corporation. It came to us through the acquisition and merger with Integrated Genetics, a company known for its leadership in the research and diagnosis of cystic fibrosis. Our strategy incorporates a combination of acquisition and organic growth. The measure of our success has been our emergence as a leader in complex testing services: initially in the reproductive area and now in oncology. This strategy underscores our belief that the combination of diagnostics and therapeutics, linked together, will enable physicians to deliver improved patient outcomes in a cost effective manner. This is core to being a responsible health care company.

Genzyme is also committed to patients with rare and complex lysosomal storage disorders, where it is absolutely essential to obtain an accurate diagnosis prior to starting therapy. In this context, the personalized medicine approach ensures that the right patients receive the right therapy.

WHLE: At first brush, personalized medicine fits into the Genzyme business model in that it meets an unmet need for better information. Can you give an example of this in practice?

MGA: It is an unmet need for information, and it is core to the fundamentals of our business model. Our very specific drugs can only and should only go to those who are clearly diagnosed. We are increasingly involved in oncology. For cancer patients it is not only about initial diagnosis, but also about understanding and monitoring their response to treatment. A good example is our test for minimal residual disease for patients with chronic lymphocytic leukemia (CLL). The patient may be receiving one of Genzyme's drugs, Campath, and we

can test to determine whether the drug is working by measuring the level of residual cancer cells. You can ask, 'Do I need to do one course of the drug, or do I need to do two courses of the drug?' It gives the physician the data required to provide the most effective course of treatment for the patient. If you broaden that example, it provides a significant change from the current system: trial and error medicine, to a system that has truly personalized medicine.

What is essential is that diagnosis is where it all starts. You need an accurate and timely diagnosis in order to best treat an individual patient or group of patients. While nothing replaces the clinical judgment of a physician, the clinical exam alone is often not enough to make a clear diagnosis. So what we are here to do, through our extensive diagnostic services and products, is to give the physician the information they need to make an accurate and timely diagnosis. This is essential to providing appropriate treatment. If you look across all drug categories today, an average of 50% of people treated with individual drugs are receiving treatments that are not efficacious for them. The critical factors are a need for timely, more specific and more accurate diagnosis.

"If you look across all drug categories today, an average of 50% of people treated with individual drugs are receiving treatments that are not efficacious for them."

WHLE: How might your tests affect the competitive environment for drugs that are not in the Genzyme portfolio, such as the EGFr inhibitors Iressa and Tarceva?

MGA: For those two drugs, our CLIA-certified, independent, analytic test reports detailed mutation status, providing the physician the information necessary to pick the most appropriate first line therapy. Compare this approach to traditional trial and error medicine, which says first line of therapy is X, and second line of therapy is Y, and third line of therapy is Z. Now, you have data that says the third line therapy might be disproportionately likely to work in this patient.

Cancer patients typically do not have the time to wait to try line one and line two before they get to the third line, which may be the most appropriate treatment. This is particularly important in cancer because of the focus on improving survival rates. The one year survival of lung cancer patients with either small cell or non-small cell is 35-40%. Five year survival: 6-13%. If there are patients who are alive at one year but not alive at five years, we are giving them a therapy that could save their life and increase their five year survival. That is what we need to do. Herceptin does the same thing. For women who test Her-2 positive, it has now become the standard of care to immediately treat with Herceptin.

WHLE: The Campath and EGFr examples are interesting in that you have a test that might actually tell you not to treat a patient. If you look at pharmaceutical companies in the aggregate, there is a fear that personalized medicine might actually reduce their market sizes. Why is it that Genzyme is jumping into this arena?

MGA: You are right in that there is still a lot of fear in the marketplace around personalized medicine. From a pharmaceutical industry perspective, the perception is one of a decreased market size. I take a very different view of that. The question is, what is the definition of market? In my mind, a market is limited to those people who will benefit from the drug. For many areas and many classes, the market is already made up of people who will not benefit from a particular drug as a result of the historical trial and error approach. If you look at classes of drugs, ACE inhibitors: maybe 10-30% of people are getting no benefit; beta blockers: 15-25%; anti-depressants: 20-50%; statins: 30-70%; beta agonists: 40-70%. We need to do better for our patients. And that says to me that the market, as it is defined today, is not accurate.

The question is how do the pharmaceutical companies best use the very powerful drugs that they have? In my mind, they do that by targeting those who will most benefit. For virtually everyone there is the opportunity for tremendous benefit, but we have to do a better job linking patients with specific drugs through personalized medicine. Not only will we reduce costs to the system and reduce adverse events, but I suspect we will get much higher compliance because the patient recognizes when a drug is doing some good or not.

The figures on compliance are broad. I have seen anywhere from 30% non-compliance to 75% non-compliance. If you had a smaller market size in terms of number of people but much higher compliance, the actual decrease in market size might be far less than perceived. In addition, from a pharmaceutical company perspective, you might have a reduction in clinical trial

cost. Great idea, some of the estimates are upwards of $100-130 million. But in order to do that, you have to be thinking about your subpopulation early in the development process.

WHLE: Will the reluctance of pharmaceutical companies to commit resources to personalized medicine delay the impact it might have on medical care?

MGA: I do not think pharmaceutical companies have a choice. Personalized medicine is here today. Personalized medicine is not going away. Personalized medicine offers us the best hope to improve the health of patients while at the same time reducing costs. So, what I think will need to happen is that the health care industry as a whole will need to take action.

I believe managed care organizations will insist that a clear and accurate diagnosis is established for disease before they will pay for a drug. I believe the FDA will get involved. Just a year ago, Mark McClellan said that instead of having 10-20% success rates over a broad population, we want to get to 80-90% benefit with fewer side effects. The only way to do that is through clear and accurate diagnosis and monitoring combined with identifying appropriate therapeutic choices for physicians. I believe that is what is going to happen moving forward to ensure that we are getting better treatment. I also believe that as soon as something becomes the standard of care, people do not call it personalized medicine anymore. I think that is actually good news. Gleevec is not used as an example of personalized medicine because it is the standard of care. My vision of the future is that personalized medicine will simply become the accepted practice of medicine.

WHLE: The issues impacted by personalized medicine (high health care costs, ineffective drugs, expensive development, adverse events) are all central to the problems with the current health care system. Is personalized medicine one of the solutions to the crisis?

MGA: Personalized medicine is an evolution. This is the next step in a process that will make us all healthier and, I believe, more economically efficient. We need to embrace personalized medicine, not just tolerate it, so that we can use all that knowledge and move to the next level of effectiveness. The system today works very well. The average life expectancy has risen tremendously. The number of people who can live healthy, high-quality lives without pain is at its highest, but we should not rest on our laurels. We need to take it from where it is today and improve upon our improvements. Personalized medicine is the key way to do that. We are all patients. We do not want to be sick. We want to figure out what we have and get better quickly using very focused drugs.

Traditional medical treatment is observation, action, and observed response - repeat as needed. That is trial and error medicine. Personalized medicine and medical care in the future is observation, test, action, and predictable response. If we do that right, repetition will not be needed. That will be the definition of traditional medicine in the future. Physicians will get involved before there are irreversible symptoms and before a tremendous amount of time and energy has been expended. This will bring the dual benefits of reduction in costs and improvement in health.

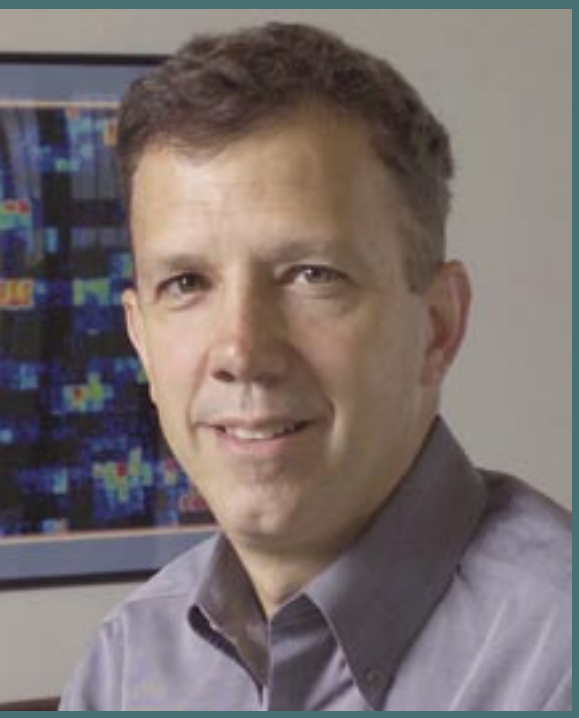
"I do not think pharmaceutical companies have a choice. Personalized medicine is here today."

The health care system is currently burdened with drugs that are not as effective as they could be, high rates of non-compliance, adverse reactions, and withdrawals from the market. The industry is not being perceived as it should be: as a key contributor to all the positives that have happened in health care. Using personalized medicine, we can have more focused and effective treatments. I believe that personalized medicine will improve the public perception of the pharmaceutical industry and the effectiveness of the entire health care system.

WHLE: Over what timeline do you believe that personalized medicine will exert its impact on the practice of medicine?

MGA: I believe it is here today. Like all change in the medical industry, physicians and companies want to take it slowly to ensure that a new system, a new paradigm, is not doing any harm. I think that is fair, but we as an industry need to pick up the pace, overcome the fear of the negatives, and move forward. As a society we cannot afford the status quo: health care costs are going up, patients do not have time for the status quo, the industry is losing patients to the status quo. ■

THE CHALLENGES THAT REMAIN



LEE E. BABISS, PHD, is vice president, Preclinical Research and Development for Roche in Nutley, NJ, where he is responsible for developing and directing oncology, metabolic diseases and inflammation research strategy. In addition, he is a member of the International Research Management Team, which develops global research strategy; chairs the Roche Biomarker Leadership Team, a cross-divisional effort within the company's pharmaceuticals and diagnostics divisions aimed at developing and implementing a biomarker strategy; and also chairs the Roche R&D Center China Scientific Board. Prior to joining Roche, Babiss was vice president of Biological Sciences and Genetics at Glaxo Wellcome, where he focused on the development of antisense technology and cancer therapeutics; headed the Department of Molecular Cell Biology; and played a key role developing and implementing the Cell Cycle Program. Babiss also served as a member of the US Research Senior Management Team, which formulated and implemented Glaxo's US research strategy and was involved in creating the Glaxo Wellcome Corporate Genetic Strategy, leading to the creation of the company's Genetics Division. Babiss attended graduate school at Columbia University, College of Physicians and Surgeons, in New York, where he earned his PhD in Microbiology in 1982 studying DNA tumor viruses.

Here, Dr. Babiss reflects on the challenges ahead for personalized medicine. He argues that while the personalization of medicine is simple in theory, successful execution remains a scientific and business challenge. Despite these complexities, he argues that it is imperative that companies continue to pursue this research because it promises to fundamentally change the practice of medicine.

WHLE: What is your perspective on Roche's research activities in personalized medicine?

LEB: At Roche we have been very pragmatic in our approach for the last seven years. We have collected samples from our clinical trials. In some cases we have collected serum and obtained RNA. When appropriate or possible, we have collected tumor tissue samples in our oncology trials. This has been done under GLP, and I would say the bulk of that work is focused on retrospective (versus prospective) analysis.

In parallel, we have put in place the appropriate team with specialists in genomics, medical genetics, public policy, regulatory, all of the areas you can imagine would be impacted by uses of personalized medicine applications. Every program in our portfolio has a strategy in place. Each strategy could be very complex and could call for the use of markers and patient stratification early in clinical development. At the other extreme, the team may sometimes feel there is no need for personalized medicine application.

The advantage that we have as a pharmaceutical company is that we are also the largest diagnostics player. So, when we are in the early stages of developing analytes or biomarkers, we can work with our diagnostics colleagues to generate the appropriate assay format with the appropriate sensitivity and specificity. The diagnostics division, if appropriate, can bring that analyte or biomarker to market.

However, the market opportunities for drugs and diagnostics are very different. Overlap across the opportunities is maybe not as significant as one might expect. We have broken down clinical biomarkers into five categories.

I. Risk Assessment Markers are markers that could be used to assess an individual's risk of developing a disease. A good example would be BRCA1/BRCA2

for the prediction of breast cancer risk. There is a strong business case for the diagnostic side of it, but there is sometimes limited opportunity for preventative measures on the pharmaceutical side.

II. Screening Markers are markers for people that are still asymptomatic but at high risk: age-related risk, familial risk, or environmental risk, of developing a specific disease. There is a strong case for this on the diagnostics side, but not so much on the pharmaceutical side.

III. Prognostic Markers aid in predicting what the course of disease will be from diagnosis. For example, when an individual is diagnosed with cancer, we can stage the cancer and see how likely it is that the cancer will progress into a highly invasive disease. This informs the aggressiveness with which the disease is treated.

Then we get into an area which has a strong case for pharmaceuticals but maybe not so much for diagnostics:

IV. Stratification Markers are markers used to help choose the best therapy for the patient based on either the nature of the disease or on the patient. The problem with these on the diagnostic side is that they are typically one-off uses. Thus the market opportunity depends on the prevalence of new occurrences as use of the diagnostic is usually limited to that drug or drug class. On the pharmaceutical side, this is really the whole basis of personalized medicine: to choose the best therapy for the patient.

V. Therapy Monitoring allows us to monitor the activity of the drug against the disease itself, either looking at reduction in symptoms or recurrence of disease symptoms. In this area there is good overlap between pharmaceuticals and diagnostics because they must be used in tandem.

WHLE: It seems as if your strategy is based on the promise of personalized medicine. Which is to say: if we want to do personalized medicine later, we need to do the research and the tissue collection now.

LEB: There are certain pragmatic things we do, sort of like building a stadium: you build it, hoping they will come. The precautionary collection of samples is done for that purpose. There are several instances now where drugs on the market have been bumped. Where we have seen liabilities in those products, we are able to go back to those samples and try to tease out the molecular basis to solve the problems. That is a very valuable resource. However, I am not convinced that is the true essence of personalized medicine, because I think it is very difficult to resurrect failed drugs using this approach.

We are faced with the reality that on average our drugs work well on probably about 30-40% of the patients that take them. The other 60-70% of patients receive minimal or no benefit or have adverse reactions. We believe there has to be some molecular basis for that differential response. We believe for some of our drugs we can address this issue by applying personalized medicine in a clinical setting in the treatment selection phase.

"We are faced with the reality that on average our drugs work well on probably about 30-40% of the patients that take them."

WHLE: This approach appears simple in theory, what are the key scientific challenges?

The challenge is that we need to come up with a hypothesis prior to going into the clinic. Let's say we come up with a dream of an analyte. What you will find is that you would probably not apply this test in a Phase I clinical trial because you are not dealing with actual patients except in oncology. Now we move on to Phase II. In Phase II, what you are trying to do is find a no-effect dose or adverse event (toxic) dose and a maximum effective dose. When you break those into cohorts, you are probably looking at 10-20 patients in each of those cohorts, which is not enough power to convince you that there exists a cause and effect relationship between the biomarker and the patient's pathology. So, now you move into the Phase III studies, and you cannot use that information to stratify them. But, what you could do in parallel is apply the use of those biomarkers as an entry criterion.

There was a naïve belief that you would get sufficient prospective data out of your Phase II trial that would allow you to stratify Phase III and do smaller trials. That was flawed for two reasons: 1) In the Phase II trial, you are not going to have sufficient power. 2) In Phase II what you are trying to do is expose as many individuals to your drug as possible to get a feel for safety. That has nothing to do with efficacy. So, if anything, you are going to add another arm to your trial and increase your cost. That arm will be focused on the personalized medicine. A second belief is that you would have sufficient data to register the diagnostic and

pharmaceutical product at the same time. The answer there is 'maybe, but probably pretty rare.'

WHLE: Is this process, as resource intensive as it appears to be, restricted to Big Pharma?

LEB: It is not really resource intensive because, in most cases, the collections that we are doing for the patient to monitor all their analytes will be applicable to monitoring the novel analytes that could be applicable to personalized medicine. So, actually, the incremental cost is not significant. In the retrospective case, your market experience allows you to know the differential response, to know there is a potential liability with your drug, or to know you can improve efficacy and safety. Thus, you can generate hypotheses, create the analytes, and begin testing. The good news is that you have Phase IV trials taking place, so you have access to patient samples at no extra cost.

"Personalized medicine changes clinical practice and evolves clinical practice, but it is not simple."

The challenge here is on the business side. Now you have a drug that is being widely used, and you may want to reduce its usage. The other truism that emerged is that you can do this and you may be able to capture a greater share of the market and charge a premium because of greater efficacy. In most markets that is probably not correct. Once you come to the market with a price in administered price settings, it is very hard to move that price dramatically based upon data like this. So, there is reluctance on the business side to do these types of studies unless absolutely necessary.

WHLE: What impact do you believe personalized medicine has had and will have on pharmaceutical companies and the market in general?

LEB: Quite honestly, the whole area of personalized medicine emerged at a time in the industry where there was a huge gap in the pipeline. The question was, 'how could you cover that gap and still sell a good story to the analysts?' This created a lot of hype because it is a beautiful story to tell. It was not malicious. It was a true belief. But, I think once you move from the area of creating hypotheses to actually doing the work, the reality of the situation kicks in. It is very important to do all this work, but the success in terms of products in the market will be rather limited.

I think there have been two lessons that have had an impact on us. On the diagnostic side, the rules have changed. It used to be that you put an analyte out there and let the clinicians figure out how to use it. Those days are over with the advent of evidence-based medicine. Most of the diagnostic companies are not geared up to do clinical trials to show the value of their diagnostics and since tests are rarely reimbursed based on value there is little incentive to make those types of large investments.

The example for us is the P450 chip that we have on the market. We put out a chip with two polymorphic P450s, which are known to have an impact on the activity of a wide variety of drugs. The problem is that while this is well known, neither Roche nor anyone else has done the prospective studies that payors want to see. We are currently, however, pursuing collaborations to address this.

The second problem is convincing the physicians to change their clinical practice. A number of anti-depressants are metabolized by P450s. If a patient takes the pill and has a minor adverse reaction, the physician will instruct the patient to only take half of a pill. If the patient is fine after a couple of days, the physician thinks, 'what do I need a test for?' Personalized medicine changes clinical practice and evolves clinical practice, but it is not simple. I think that is one of the areas that is confounding for us on personalized medicine.

WHLE: When faced with all these challenges, will personalized medicine fail to bring on the promised revolution in health care?

LEB: It is an evolution. If you look at our ability to discover new medicines over the last few years, there really has not been a lack of productivity. Rather, there has been a lack of success measured by the number of launches of new drugs. Type II diabetes, cardiovascular disease, rheumatoid arthritis, asthma, are polygenic diseases and are strongly influenced by environment, as well. Our single-target approach to these diseases has not proven to be terribly good.

We have had to learn in the clinic, fail in the clinic, and go through several iterations. I do not see personalized medicine being any different. It is about generating hypotheses, testing them and accepting that there is going to be a large failure rate because human biology is very complex. That should not sway you away from doing it. You still have to do it. All of the companies are investing significantly and appropriately in this area because the impact is not just on personalized medicine, it is on medicine and drug discovery in general. It is going to be an evolution; it is not going to be a revolution. ■

REGULATING THE TRANSFORMATION

LAWRENCE J. LESKO, PHD, has been director of the Office of Clinical Pharmacology and Biopharmaceutics in the Center for Drug Evaluation and Research at the Food and Drug Administration since 1995. The main focus of Dr. Lesko's Office is the analysis of dose-response and PK-PD data for the purpose of optimizing dosing of FDA-approved drugs, the use of biomarkers to assist in dosing adjustments for drug-drug interactions, special populations (e.g., renal patients) and patient subsets defined by genomics, individualization of drug therapy, and the application of quantitative methods resulting in disease state progression models and clinical trial simulations. Dr. Lesko is chair of the FDA Pharmacogenomics Working Group and the Clinical Pharmacology Section of the FDA Medical Policy Coordinating Committee. He serves as president of the American College of Clinical Pharmacology and is an American Association of Pharmaceutical Scientist (AAPS) fellow. Dr Lesko is Board Certified in Clinical Pharmacology by the American Board of Clinical Pharmacology.

Here, Dr. Lesko discusses the regulatory environment for the development of personalized medicine products. He describes how the FDA has created a regulatory pathway to facilitate the early development, submission and review of pharmacogenomic data for targeted therapies. Dr. Lesko anticipates a significant increase in the number of personalized medicine products over the next five years and expects regulatory agencies to be major players in facilitating the introduction of these products to the marketplace.

WHLE: What steps has the Agency taken to speed innovation in pharmacogenomics and what is the Agency's role in advancing the field of personalized medicine?

LJL: The Agency's role has been, in the context of its leadership in public health, to advance any technology or tool that would improve public health. That includes genomics. Its leadership role is primarily focused on improving public health through individualizing therapy in patients and patient subsets and facilitating drug development. As part of an agency-wide initiative to speed development of new medical products through the science of pharmacogenomics and biomarkers, the Agency issued a guidance in March 2005 titled 'Genomic Data Submissions.' We have tried to facilitate the growth of this area so that it can realize its potential. However, we are doing so in an incremental manner that is based upon the scientific evidence that comes before us. As you are probably aware, there has been a lot of perceived exaggeration and a lot of under-delivery of pharmacogenomics. I think the Agency's concern is to keep a balanced view of this by focusing on progress.

WHLE: What do you think is the cause of this under-delivery?

LJL: There are certain considerations that companies go through in thinking about genomics. One might be an economic fear that tailoring a drug to a subset of the patient population may reduce market share. I think we have moved through that fear by virtue of the large market shares that personalized medicine has acquired through drugs like Herceptin. Thus, there is a model out there with Herceptin that shows that companies do not need to worry about small market share if they bring patient value to the marketplace.

From our standpoint at the FDA, I think we realized in 2002 that the 'fear' companies had expressed revolved around: 1) What exactly is the FDA going to do with this data? 2) Is it going to trigger requests for more research? 3) Is it going to force us to develop diagnostics? and 4) Is it going to restrict our indications

and our market share? I think there is still fear around all of those questions, but it has declined significantly since 2002.

WHLE: How has the Agency partnered with industry to alleviate this 'fear' and facilitate the integration of pharmacogenomics into drug development?

LJL: I believe the reason for the significant decline in this 'fear' is the guidance that we put out in March of 2005 on genomic data submissions. That was a guidance that simply said, 'Here is what we are thinking and here is a process by which you, the company, can voluntarily submit genomic data to the FDA for the purpose of exploring questions about how it would be used in drug development.' Since the guidance came out, we are now up to 25 voluntary submissions. I believe companies have left the meetings pertaining to voluntary submissions with a lesser concern about what the FDA is going to do with these data.

"I think when people look back on the progress of pharmacogenomics and targeted medicine they will be impressed and surprised that we have come as far as we have to date."

WHLE: What about integrating pharmacogenomic data into regulatory decision-making? How will the Agency use such data to evaluate products in the future?

LJL: The decision making that goes on in a regulatory agency asks several questions, one of which is, 'Does the drug work?' And there are standards for that (i.e., two clinical trials showing evidence of effectiveness based on a P-value<0.05). Another question that is asked is, 'Is the drug safe?' Of course 'safe' is a relative term. There are actually no regulatory standards for drug safety. The decision to approve a drug is based on the relative benefit and the relative safety of the drug (i.e., the benefit-risk ratio).

I can imagine the way regulatory agencies would use genomics in the future would be to take a benefit-risk ratio and begin to better understand variability in the drug response, since that ratio is dependent upon differences between individuals in their response. For example, if the drug does not have an acceptable benefit-risk ratio, one could use a genomics test to predict drug safety and reduce the denominator so that the benefit-risk ratio becomes more positive.

I think the point of view that regulatory agencies (not only the FDA, but the European agency as well) will have in the future will be, 'What is the underlying cause of the differences in the way people are responding to this drug?' This will not necessarily lead to personalized medicine, but it will lead us to think about it in a more individual patient-oriented way.

WHLE: What role do you think personalized medicine will play in previously-approved drugs? Is it likely that the availability of new pharmacogenetic data might change the benefit-risk assessment and trigger a review of previously-approved drugs?

LJL: In the area of previously-approved drugs, we need to think about their history in terms of benefit and risk. It is certainly conceivable as we have seen with some drugs that are metabolized by enzymes with genetically-determined activity: the thiopurine class of drugs (with TPMT as the enzyme), irinotecan (with UGT 1A1 as the enzyme) and warfarin (with CYP 2C9 as the enzyme). There is not a long list of marketed drugs like this, but there are perhaps one or two more such drugs that we might want to look at in the future. Of course this initiative all depends on the availability of new genomic information.

It is always going to be a challenge with older drugs because the medical community is used to working with them. It is difficult because they are, in most cases, off patent so that the prospects for companies to improve benefit-risk are modest.

WHLE: What are the implications for personalized medicine for drug development?

LJL: We have to think about the drug development process as we currently understand it and then think about what changes will occur as the science of genomics matures. If you begin at the front end of drug development, I think one of the first things that will change in the future will be a better understanding of the disease biology or, as some people call it, disease pathophysiology. We see this happening exclusively in cancer: we begin to understand tumor biology and as a result we begin to understand drug targets and biomarkers that are indicative of the biological receptors (e.g., site of action) of disease and the disease process. The next step is to develop a drug that targets that

receptor and from there test the hypothesis of efficacy in the patient population. There are many case studies in oncology (e.g. Herceptin, Tarceva) that give insight as to how the future might change for other diseases.

But I would also like to point out that there are two sides to a coin in genomics. What I just talked about is the head of the coin (i.e., understanding the genetics of disease biology in order to evolve into personalized medicine). The tail side of the coin is what I would call dose-response genetics. If I have a drug whose pharmacokinetics or pharmacodynamics are influenced by genomics (such as warfarin), then it makes sense to use that information to optimize the dose that you are going to use in patients. And that is equally attractive in terms of impact on public health. Getting the dose right and getting the drug right go hand in hand. We have used that philosophy in the way that the Agency has advanced genomics for older, marketed drugs as well as newer, to-be-approved drugs.

WHLE: What challenges do you foresee the medical community facing in transitioning from the use of generalized medicine to personalized medicine?

LJL: The practice of medicine is a spectrum that at one end is the general practice of medicine and at the other end is what we call personalized medicine. In between are practicing physicians, who in many cases are individualizing medicine to the extent they can, using experience and individual patient information (e.g., age, family history) that has traditionally been available. As you move along that spectrum of medical practice, the question really is, 'how targeted can therapy become, through genomics, to enable one to actually practice the personalized medicine scenario?'

The first challenge is that we have very few examples of personalized medicine to date, but this is the challenge you face with any new technology trying to permeate an established framework of practicing medicine. Part of this challenge is whether there is an effective infrastructure for adopting personalized therapy. We have to worry about educating physicians to facilitate the use of the genetic test in medical decision-making. The second major challenge is whether payors and providers are willing to pay for the test. The standard for that decision is a moving target, I believe. Just what kind of evidence is necessary to warrant the payment for genetic tests is still rather vague.

WHLE: What role do you see the regulatory agencies playing to help move this transition forward?

LJL: Remember that personalized medicine is sort of at the center of a benzene ring or even a diamond with all those little points or facets sticking out. Regulatory agencies are just one of many players here. But I think that the role could be, first, to facilitate innovation in drug development that leads to the approval of targeted therapies. Second, the role could be to use the knowledge from adverse event reporting systems to begin to target drugs in the marketplace - for example, older approved drugs that would benefit from new genetic tests to improve benefit-risk ratios. Third, a regulatory agency is by its nature an advocate for optimizing public health and strives for clear information in labels to inform patients and providers as effectively as possible so that they can make the right decisions with these test results. Fourth, a regulatory agency is by its nature an advocate for a high level of test quality. I think the agencies around the world can facilitate the approval of tests by being very clear on the standards of quality (e.g., precision and predictive values) and then assuring that those standards are met.

WHLE: What about changes within the industry - do you see a similar shift in model taking place as the one you described for the medical community?

LJL: I think when people look back on the progress of pharmacogenomics and targeted medicine they will be impressed and surprised that we have come as far as we have to date. It is inevitable, I think, that the current pharmaceutical development model needs to have some changes to it based on two things:

One is the decrease in productivity we have seen over the last 10 years in terms of new chemical entities. The other is that the next 5 years will see a tremendous influx of generic drugs into the marketplace as patents expire on many of the innovator drugs. I think there is going to be a shift in the prescribing habits of physicians so that to gain value in the marketplace, a company will be required to distinguish its products (e.g., by moving them from a 'me-too' status to targeted therapies that bring added value).

So I think we are going to see a blend of strategies in industry between the continuous pursuit of 'a blockbuster' as a portion of the business and an increasing proportion of attention to targeted medicines. If we think of drug development as a pie, then the current portion that is represented as targeted therapies, which I believe is approximately 5%, will shift to more like 25-30% of the pie within 5 years. ■

India: The Rise of a Global Player

India is rapidly transforming itself from a developing world country to a robust economy with a thriving health care industry. A growing middle class with newly disposable income, increasing rates of lifestyle illnesses such as diabetes and cardiovascular disease, and the recent adoption of international patent law through the WTO's TRIPs agreement will thrust India into the forefront of the global pharmaceutical industry. We spoke with **G.V. PRASAD**, CEO of Dr. Reddy's Labs, one of the country's largest pharmaceutical companies, to understand where the industry came from and where it might go from here. We have also highlighted the Wharton perspective as we follow a **WHARTON HEALTHCARE INTERNATIONAL VOLUNTEER PROJECT (WHIVP)** team in their efforts to formulate a growth strategy for one of the most innovative hospitals in India.

INDIA BY THE NUMBERS

Number of people living in India: 1,080,000,000

Gross domestic product per capita: $3,400
Gross domestic product real growth rate: 7.1

Factor by which the infant mortality rate exceeds that of the US: 8
Factor by which the infant mortality rate exceeds that of China: 2

Annual deaths from infectious and parasitic diseases: 2,100,000
Annual deaths from cardiovascular disease and cancer: 3,730,000

Annual number of four-year engineering graduates in India: 112,000
Annual four-year engineering graduates in the US: 137,437

Years (as of publication) since recognition of patent protection on foreign drug products was abolished in India: 36
Months (as of publication) since the India began recognizing the WHO TRIPs agreement: 13

Percentage of domestic drug demand met by Indian manufacturers: 70
Number of Indian drug manufacturers: 20,000

Number of FDA-approved drug manufacturing plants in India: 60
Factor by which this exceeds the number of FDA-approved plants in China: 3

Percentage of the global population living in India: 16
Percentage of global health care investment made in India: 1

Percentage of global pharmaceutical sales in India by value: 1.8
Percentage of global pharmaceutical sales in India by volume: 8

Rank by value: 14
Rank by volume: 4

1, 2, 3, 4, 5: CIA World Factbook; 6: Population Resource Center, 1998; 7: World Health Organization, 2005; 8,9: BusinessWeek, NASSCOM, Duke University; 10, 11, 13: IMS Health; 12: Pharmaceutical and Drug Manufacturers of India; 14, 15: Burrill & Company; 16, 17, 18, 19, 20, 21: Organization of Pharmaceutical Producers of India

INDIA'S MOVE TOWARDS INNOVATION

GV PRASAD leads the core team that is driving Dr. Reddy's growth and transformation from a company predominantly selling APIs, Branded Formulations & Generics to achieving its vision of becoming a discovery-led global pharmaceutical company. As CEO and vice-chairman, Prasad has championed the globalization of the company and has played a vital role in the company's evolution. He has been the architect of the company's global generics strategy. He has helped create new platforms of growth for Dr. Reddy's in the Custom Pharmaceutical Services, Discovery Services, and Specialty Pharmaceutical segments. He has built a diverse, talented and experienced senior management team in India, Europe and the US. Currently, he is focused on driving Dr. Reddy's growth in the two largest geographies - US and Europe. Prasad has a Bachelors degree in Chemical Engineering from Illinois Institute of Technology, Chicago, and a Masters in Industrial Administration from Purdue University.

Here, Mr. Prasad discusses his views of both the branded and generic pharmaceutical business models. He argues that India is poised to become a formidable force in the global generics business and that this success and the recent changes to the business environment in India could create a launch pad for a more innovation-based pharmaceutical industry.

WHLE: Could you highlight your view of the key challenges for the pharmaceutical industry?

GVP: I think for the branded business the challenge for large pharmaceutical companies is the business model, which seems to be undergoing a change. The change is being driven by the unpredictability or the sustainability of products and revenues. As you have seen, the cost of getting a drug to the market has increased dramatically while the number of NCEs or research productivity has really not changed much. Furthermore, companies have become giant organizations. To have any impact on a company this size one really needs a very large product (or blockbuster drug). These are becoming increasingly scarce. Added to this is the fact that forces shaping the industry, particularly from the science side, are predicating a shift towards smaller, more tailor-made products that target the genetic make up of a person. Overall, the challenges are therefore increasing costs, stagnant or declining productivity measured in terms of NCEs, a lack of blockbuster drugs, and a trend towards smaller and more targeted products. When you put these all together it appears to be the time for large pharma to reexamine their business model.

In the generics business, generic manufacturers tended to be largely regional players in the past. Now you are seeing the emergence of global companies, coming in from all parts of the world. The key challenges are and will be the increasing emergence of lower cost providers from countries such as Eastern Europe, China and India. Increased price competition will impact margins, and we are already seeing companies making acquisitions (such as Teva) to continue to build scale to offset such margin pressure. However growing health care costs around the world continue to lead to ever-increasing demand for generic products and this is set to carry on in the future.

WHLE: What's your view on a branded company such as Novartis moving into the generics market, as it has done increasingly in recent years?

GVP: As discussed before, the big pharma business model is changing and clearly there will be different models and strategies to this. I do foresee fully-diversified companies in the future spanning branded, generic, medical device and so forth as there is increased convergence. The exact structure of branded pharmaceutical companies in the future is still unclear to me, but I

believe a hybrid structure will be more prevalent.

WHLE: Moving away from a global perspective and looking at India, what is your view of the state of the market at the present?

GVP: I don't believe up to now that India has been a very big innovator in the pharmaceutical business. Historically due to a lack of patent laws, companies only saw opportunities to produce generic products at a cost advantage. There was no incentive to innovate. However, we are now seeing changes, and as time goes by we will build those skills. We are seeing the emergence of a business ecosystem to enable and encourage innovation: the patent law is in place, companies like us are investing in research and doing innovative deals to finance research. However the missing links are the lack of adequate venture capital and strong academic research centers. These missing links are needed to complete the ecosystem for innovation.

"We are used to operating in a fiercely competitive price environment with severe domestic price controls which are based on the cost of production."

Coming back to the Indian industry, while we are in the early stages of innovation, we are really a force in the global generics business. We are upsetting some of the established rules of the game. This stems firstly from the cost advantages in India versus established companies overseas. There is also a history of a large number of generics players in the domestic market, which developed largely due to the lack of patents in India. This has lead to the development of a very strong national generics industry that has been replicated and furthered abroad. India is truly a world leader in that respect. We also have very strong formulation and manufacturing skills. We are used to operating in a fiercely competitive price environment with severe domestic price controls which are based on the cost of production. Due to these factors, India is in a strong position to compete in the global generics market. Clearly there are things that we can still learn, but you are already seeing a rapid ramp up of generic filings in both the US and Europe by Indian generic manufacturers.

WHLE: Do you think that a purely domestic strategy by an Indian generics manufacturer is feasible in the long-term?

GVP: Given the small size of the Indian market in comparison to the global pharmaceutical industry, it is a difficult strategy to pursue. Clearly there will always be smaller companies or niche players that are focused nationally, but I do not see any medium to large size companies staying only focused on the Indian market.

WHLE: Turning to Dr. Reddy's, what are the key focuses for you in the near-term?

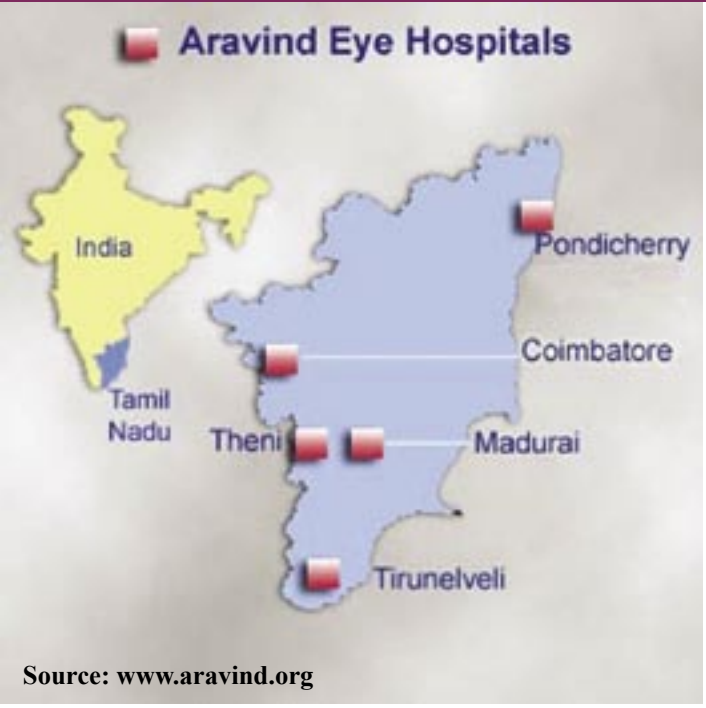
GVP: There are three key areas that we are currently focusing on for Dr. Reddy's. First, we are focused on building size to make us one of the dominant generics businesses globally. Clearly this is still a work in progress. We have established our presence in the US, Russia, UK and some smaller markets, but we are still not yet a meaningful global generics player and this is really going to be an important priority over the next three to four years. This will include building scale and entering other generics markets. The second focus area for us is building up the specialty business, which is based on innovation but not on new chemical entities. Rather, this is based on building on existing technologies and using innovation to develop new formulations to improve on existing therapies. This effort should act as a hedge against the commoditization of generic drugs and help us to differentiate beyond pure price. Finally over the last decade, we have been investing heavily in drug discovery to transform our organization over the long term to a discovery led global pharmaceutical organization dedicated to finding cures for unmet medical needs. ■

WHIVP WINTER 2005: ARAVIND EYE HOSPITALS

Each year, students from Wharton's Health Care Management Program undertake overseas volunteer work by partnering with local institutions to help improve health care in developing nations. The projects involve a small group of students who complete two to three week consulting engagements on site. This Wharton Healthcare International Volunteer Project (WHIVP) provides health care management majors an opportunity to apply classroom skills within a real-world environment while assisting the institutions and citizens of developing nations.

Overview

During the recent winter vacation, six Wharton students were involved in a volunteer consulting project for the Aravind Eye Hospital in Madurai, India. The goal was to assist Aravind in managing future expansion of its operations from the original base in Tamil Nadu, India (see map, Aravind Eye Hospitals). The initiative arose because over the past year Aravind has been involved in two managed hospitals outside of Tamil Nadu, one in Kolkata and one in Amethi (Uttar Pradesh) through partnerships with other organizations. It is clear that there will be increasing opportunity for further expansion through such partnerships and alone, hence Aravind is interested in examining which model will best achieve such expansion while maintaining the phenomenal success of their eye care services in Tamil Nadu (where over 200,000 eye surgeries were conducted during 2004 with post-surgical vision outcomes and infection rates similar to those in the West).



Source: www.aravind.org

Background

The first Aravind Eye Hospital, housing just eleven beds, was created in 1976. The founder, Dr. Venkataswamy (or Dr. V as he is now fondly known by the community) believed that reversible blindness (such as that caused by cataract) should be eliminated from the developing world. Furthermore, he recognized that the government alone could not successfully undertake such an enormous task in a developing country such as India but would need the help of the private sector. Although there was (and is) a great deal of focus on addressing communicable diseases in India, Dr. Venkataswamy realized that blindness in many cases equated to just as much of a death sentence as infectious diseases. The majority of the Indian population is engaged in subsistence farming, and a blind person, unable to work, would find themselves at best a burden to their family or at worst outcast from the community and facing starvation. This fate is supported by statistics showing that, in India, people who turn blind have an average life-expectancy of only two additional years. In the majority of cases, this blindness is reversible or could have been prevented through earlier screening.

For Dr. Venkataswamy, a patient's economic status and ability to pay are irrelevant. The goal is simply that all those requiring treatment should receive it. This has led to a unique model of health care provision that allows Aravind to provide free eye care to three-quarters of its patients using the revenue generated from the other quarter (i.e., paying patients).

Global Blindness

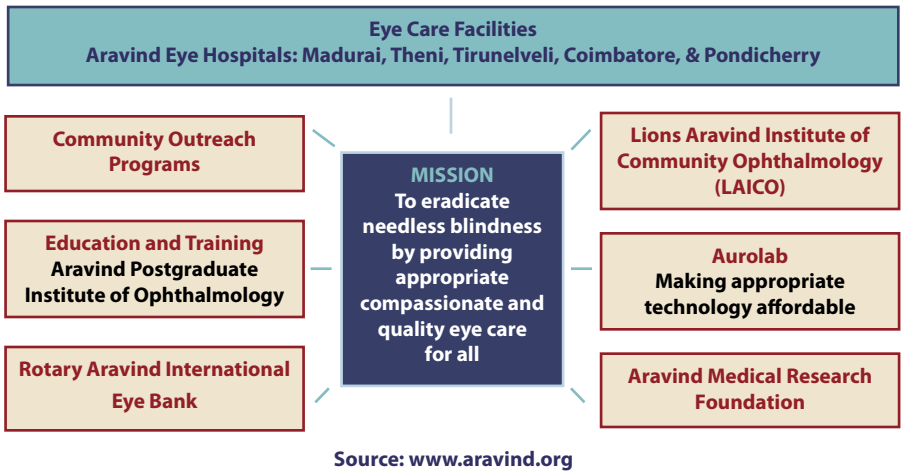
Blindness is truly an affliction of the developing world, particularly blindness that is preventable or reversible. It is estimated that, worldwide, 45 million people are blind and 180 million are visually impaired. Of this, 90% of the blind are in developing countries, with India accounting for almost 12 million - more than any other country. Incredibly, 80% of the blindness in India is due to cataract, which is almost always curable. The challenges of successfully curing this affliction in a developing country are great given the large and growing population, inadequate infrastructure, low per capita income, aging population, disease in epidemic proportions, and illiteracy. However, the reward for curing blindness is not just moral or social, but economic. Unnecessary blindness is estimated to cost the Indian economy upwards of $3 billion per year in lost productivity, and the global economic burden of blindness is around $25 billion per year. Despite the work of organizations such as Aravind, the trend points to a doubling of world blindness by the year 2020 unless more aggressive intervention is undertaken.

The Aravind Model

From the original eleven beds, Aravind has now grown into five hospitals in Tamil Nadu (the original base in Madurai plus hospitals in Theni, Tirunelveli, Coimbatore, and Pondicherry) with a total of nearly 3,590 beds. Aravind performed an incredible 228,894 eye surgeries (the majority of which was cataract) at its hospitals in 2004 and examined over 1.6 million patients. This equates to 5% of ophthalmic surgeries carried out in India during 2004, even though Aravind maintains less than 1% of the nation's ophthalmic manpower. Aravind's success is based on high patient volumes, allowing it to spread costs over a greater patient base and minimize unit costs. As a consequence, its hospitals see more patients per day than any other health care institution in the world (almost 4,000). To ensure that maximum patient volume is achieved, Aravind is geared for efficient use of resources and time management. The focus is on treating the patient with the highest level of care but in the fastest time possible time so that more patients can be seen. For example, basic cataract surgeries are carried out in 15 minutes, allowing doctors to move on to the next patient quickly and thereby maximizing surgeries per day. Interestingly, the pace of operation does not impair quality, rather the reverse, as doctors carry out more surgeries each day at Aravind than at other institutions and so become experts in their field.

Ultimately, high patient volume and cost reduction have been critical in allowing Aravind to provide equal eye care to all who need it simply by making it affordable. To support this model, Aravind recognized early on the need innovate and to engage the community. As a result, it has set up various support institutions to ensure that high volume is maintained without any compromise of quality of care. These institutions are shown in the adjacent figure (Aravind Eye Care System):

ARAVIND EYE CARE SYSTEM



Source: www.aravind.org

Aside from the core hospitals, Aravind has developed several ancillary institutions that are designed to support this unique system of eye treatment. Three have had a profound effect on the success of Aravind's model: LAICO, Aurolab and Community Outreach through camps and clinics.

LAICO

In 1992, the Lions Aravind Institute of Community Ophthalmology (or LAICO) was established to further the goal of reaching and helping the global community. The

aim of LAICO is to share the knowledge that Aravind has gained over the past 20 years with institutions throughout the developing world and transfer core competencies in maintaining successful community eye care facilities. This translates into training programs not only for Aravind's own hospitals, but also for doctors around the country and worldwide. These training programs also extend to hospital administrators.

Teams from Africa regularly come to India to be trained. When they return to their own countries and apply Aravind's model, both volume of patient treatment and quality of care rise significantly. In addition to building capacity and knowledge through training, LAICO also provides consultancy services to other institutions. This transfer of knowledge is a key element of Aravind's strategy for eradicating needless blindness throughout the world and is at the heart of Dr. V's vision. LAICO is also a center for research to examine how innovations in surgery and community care can be applied to minimize cost and maximize volume and quality.

Aurolab

Another key element of Aravind's eye care system is the establishment of Aurolab Laboratories. Prior to this, intraocular lenses (lens that are implanted into the eye following cataract surgery to restore vision) could only be acquired for over $100. This was prohibitive for the majority of the rural community, and Aravind recognized that without affordable intraocular lenses there could be no way of effectively addressing the issue of blindness. Aurolab was created for this purpose and through innovative techniques was able to develop a new method of intraocular lens production that reduced cost while maintaining quality (lenses are FDA- and EMEA-approved). Aurolab's efforts have been hugely successful, causing intraocular lens prices to fall dramatically as competitors react by reducing their own prices, thus making surgery affordable for all. On the back of such innovation, Aurolab has expanded into suture needles, eye care pharmaceuticals, blades, and instruments.

Community Outreach

Perhaps the most important element of Aravind's model has been the ability to garner community support and recognition for its efforts, which in turn has driven greater volume. Although Aravind does no formal marketing, it reaches rural communities (which can be over 30 miles away from the hospitals, themselves) through eye camps. These camps are organized by community leaders that have often had a long standing relationship with Aravind (some leaders have organized over one hundred camps) with the help of Aravind facilitators. The camps are located in halls or school buildings within a rural location and attract people from miles around. Typically, the camps are held once every three months (though frequency can vary from monthly to once a year). In order to alert people about the camp and provide details, handbills, megaphones and posters are used for publicity. In 2004 there were over 1,200 camps, which saw approximately 430,000 outpatients and referred 95,000 patients for surgery.

The importance of these camps cannot be overstated in an area such as Tamil Nadu, where the majority of the population lives in the rural areas. These camps provide a mechanism for providing care to the rural community and ensure that the community is screened regularly to help detect eye problems early. People that require surgery are referred to the nearest hospital and will be taken that same day in one of Aravind's buses for free. Speed of delivery of these patients to a hospital setting is critical as patients, when given time to think about surgery, often change their minds even though the benefits are clear. All patients coming through these camps receive surgery for free as they cannot afford to pay. Other services, such as glasses, can also be provided for free depending on the patient's ability to pay.

Innovation and Technology

Aravind's success is due not only to high volume, but also to continuous technological innovation to ensure that the health care system is aligned with its goal of high quality care for all. Aravind has successfully adopted technologies to complement its high volume system and to reach patients in rural India. An example of this is a tele-ophthalmology system which allows doctors located at the central hospitals to talk to and see patients in rural areas using teleconferencing equipment. Aravind routinely sends buses out to rural areas with the teleconferencing equipment and uses satellite technology to target rural pockets where populations are densest, allowing more patients to be treated by a single bus.

A second example of Aravind's bold use of

innovation has been in the area of glasses. Previously, patients would have to wait a long time to receive glasses once they had ordered them from eye camps. They often would need to return if there were problems with the fittings. These delays, plus the cost, meant that many patients would decide not to bother ordering glasses at all. Aravind realized that this could be improved and developed a system to shape and assemble glasses at the rural site in just 30 minutes. This cut down the patient wait time from weeks to just hours and reduced costs as Aravind carried out the work itself.

WHIVP

Aravind has been looking to expand its hospital base in India and other developing countries to achieve its mission of eradicating needless blindness across India and around the world. At the same time, Aravind's growing reputation has meant that more and more NGOs and partners (industrial, political, etc.) within India are turning to it with requests to manage their state's eye care institutions. The question they face is whether to expand via managed care hospitals (with partners such as in Kolkata or Amethi) or whether to expand alone. While the former allows the risk of entering a new region to be shared and mitigated through the partner, the latter model gives Aravind better control over the management of hospitals and therefore more chance of replicating its success in Tamil Nadu.

The role of the WHIVP team was to help Aravind examine these options as well as to develop a series of operational and financial metrics that would be used to manage the growing network of hospitals. The project entailed analyzing Aravind's current model and synthesizing a recommendation around the organizational implications and requirements of managing an increased number of hospitals. The project itself was broken into three phases. Phase one consisted of a situational assessment to develop an understanding of the key issues and the value drivers of the Aravind model. This involved meetings with the senior management of Aravind as well as hands-on experience at each of the facilities including the surgical units, eye camps and Aurolab. In phase two, the team analyzed the internal operations of the hospital network, developed an understanding of best practices for hospital network expansion based on appropriate benchmarks, and created forecasting tools to anticipate the implications of each expansion alternative. Finally, phase three synthesized these results into a formal presentation of recommendations to Aravind senior management. ■

WHIVP Team (from left Anil Saggi, Puja Gupta, Zachary Treuhaft, Anup Swamy, Pete Hultman, and Brian Craig)

Special thanks to the dedicated staff of the Aravind Eye Hospitals.

HEALTH CARE SYSTEMS OF THE FUTURE

JOHN R. KIMBERLY, PHD, is the Henry Bower Professor at The Wharton School and the Salmon and Rameau Fellow in Health Care Management at INSEAD in Fontainebleau, France. His research, teaching and consulting focus on issues of organizational change and innovation and their impact on corporate performance and individual careers. Dr. Kimberly is a founder and principal in the Executive Careers Institute, a global research firm that conducts research, develops educational programs, and provides consulting on executive careers and the changing nature of the connections between people, work and organizations. He and his colleagues have written widely on issues of innovation and change in the workplace. His articles have appeared in the Harvard Business Review, the Administrative Science Quarterly, the Academy of Management Journal, Les Echos, and a host of other academic and practitioner publications. His most recent book on health care, The Quality Imperative: Measurement and Management of Quality in Health Care, written with Dr. Etienne Minvielle, was published in 2000 by the Imperial College Press in London. He is currently working on a book with Professor Hamid Bouchikhi on the subject of organizational identity and its influence on processes of organizational change.

Few people would argue that the future is a sure thing and never more so than when trying to predict changes in the health care industry. Here, Dr. Kimberly shares some of his thoughts on what the health care system of the future may look like based on his research and experience with the health care value chain in this country and around the globe.

WHLE: How will the role of the patient change in the future?

JRK: We are likely to see the patient at the center of the health care system, playing a much more active role in meeting his / her medical needs. The patient will have access to various sorts of information to aid with the decision-making process. The idea here is, and we have already seen elements of this on the horizon, that patients are going to have access to a variety of types of electronic information not only about themselves and their health status, but also about options and alternatives that are available to them. We can identify three major types of information that will become readily available: first, there will be data about the patient's own condition, biological parameters, medical history and so on. Second, there will be links between research and knowledge about disease and disease course that patient will be able to access. Third, there will be information about services or treatment options that the patient will be able to access, sometimes with the help of intermediaries. In instances where the patient has difficulty understanding that information, there will be the need for intermediaries who will guide them through the choices they have to make.

WHLE: Can we expect similar changes in information availability on the care side?

JRK: Yes, on the care side we would expect to see substantial benefits from systems with real-time clinically relevant information such as medical histories of any given patient and updated medical research on any topic at the touch of a button. We can think of this as electronic pathways that touch all parts of the health care system. We will have a system where the flows of information among different units (if all goes to plan) will be virtually instantaneous, reliable, secure and complete.

WHLE: What can we expect of hospitals in the future?

JRK: The hospital as we have known it will change radically over the course of the next 25 years. Hospitals in the future will take on a much narrower, but even

more important function, as solely acute care institutions and centers of medical information. They will strip out as much of care as can safely and logically be provided in other lower cost settings, and they will focus their clinical expertise more.

The acute care facility will be very high tech and much more limited in scope than it is today or has been historically. And the name of the game will be to send as few people to those facilities as possible, making sure that there is a good fit between patient needs and what that facility offers.

WHLE: What about the non-acute care cases? Where will they go?

JRK: As hospitals become more acute care focused, we will find organized alongside a number of alternative settings for care, some of which will be quite specialized. This is what we call 'focused factories' where particular conditions will be treated. Shouldice is a well-known example: they do nothing but hernias; they are geared up for that and as a result they do hernia repairs better than anyone. Some of the facilities around the acute care center will be focused factories, while some will be the equivalent of step-down facilities where patients will go after hospitalization for post-operative care or intermediate level care such as having an IV maintained. They do not need to be in that acute care facility because that is so expensive, so we will need these step-down intermediate care facilities.

We will also have another set, and I do not know if they will be physical buildings or just capabilities in the community, which will link the patient to various kinds of care options. These will have a public health flavor to them, so people who have issues around obesity, substance abuse, or social illnesses can get help. They will be entities of first instance that will be responsible for trying to maintain the health of a given population in any given community. So what we will have, I think, is a system that is much more highly differentiated organizationally than it is today. And of course you and I will have a range of diagnostic, monitoring and health maintenance capabilities available where we live, connected to the rest of the system electronically. [See an organizational framework for Dr. Kimberly's ideas on page 42.]

WHLE: What leads you to believe these changes can occur?

JRK: A friend of mine visited the Hospital of the University of Pennsylvania (HUP) recently to have a test done, and he was in a unit of HUP that had never seen him before, but at the touch of a button they had all of his previous information. Imagine that, not just at the level of the hospital, but available much more widely. Clearly, there are a lot of questions surrounding security and privacy of that kind of information that need to be worked out, but it will come. My vision is that health care will be provided in a much more efficient and much more effective way in this evolutionary / evolved model than it is today. And that model is going to have different kinds of training requirements, different kinds of personnel, particularly for those units that are going to mediate between citizens / patients on the one hand and the more intense technologically sophisticated parts of the system.

"Technology will be the biggest enabler; technology is what is going to allow this to happen."

WHLE: Do you see technology issues as the biggest challenge?

JRK: I think technology will be the biggest enabler; technology is what is going to allow this to happen. I think the biggest obstacles or challenges will be two-fold: one is financing, how the financing and insurance side is going to work. Second is the evolution of these organizational entities alongside the hospital. There is an awful lot of inertia built into present arrangements, as they serve people's interests well. It is going to be a challenge to move those. I think the driver will be technology and technological capabilities both in information technology and in medical technology. When you think of all the things that are happening in both domains today, it is not much of a stretch to imagine things moving inevitably in this direction.

WHLE: Will pressure from patients, who will demand increasing information, uptake of technology and higher quality of care, also drive this forward?

JRK: One would certainly hope so, and current developments strongly suggest that this is not a romantic view but that it is highly likely. Amid all the uncertainty about the future, however, on thing is absolutely clear. Technology and know-how will continue to drive changes in health systems around the globe. ■

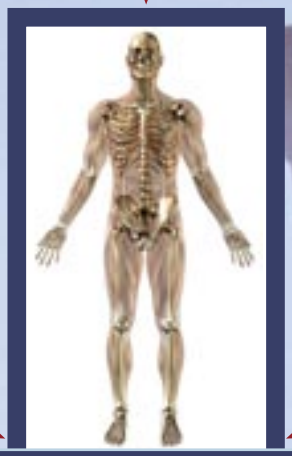
AN ORGANIZATIONAL FRAMEWORK FOR THE FUTURE

HOSPITAL
- **Acute Care**
- **Data Aggregation Hub**
- **High tech center**
- **Limited in scope**

Information updated real time

Information updated real time

SPECIALIST CENTERS
- **Focused by therapeutic area**
- **Post-op care moved to step-down**



STEP-DOWN FACILITIES
- **Post-operative care**
- **Non-acute hospitalization**

PATIENT INFORMATION
- **Personalized medical history**
- **Medical research and knowledge**
- **Services available for treatment**

Information updated real time

Information updated real time

PUBLIC HEALTH INTERMEDIARIES
- **Community-based capabilities**
- **Link patients to care options**
- **Clinics (e.g., for obesity, substance abuse)**

Wharton Health Care Business Conference

The Wharton Health Care Business Conference celebrated its 11th year by focusing on the exciting innovations that will shape the future of human health. As the leading health care business forum for industry professionals, academics, and students, the Conference is at the forefront of industry thought leadership. The annual two-day event takes place every February in Philadelphia, PA, and typically draws over 500 attendees including students, professionals, and academics from across the nation. Corporate sponsors fund the Conference operations. The 2006 conference was held on February 16th and 17th at the Park Hyatt Bellevue in downtown Philadelphia. A full description of that event's agenda and participants can be found at www.whcbc.org.

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"The Wharton Health Care Conference is not just the best conference organized by students, but one of the most impressive gatherings of industry leaders tackling timely and important issues in the health care industry." - *Stelios Papadopoulos, PhD, Vice Chairman, SG Cowen*

Wharton Health Care Club

The Wharton Health Care Club organizes professional, academic, and social activities for all Wharton graduate students who are interested in exploring opportunities in the health care industry. Members share their curiosity and experiences regarding current issues facing hospital, physician, managed care, pharmaceutical, biotechnology, and medical device organizations. The Club seeks to educate the Wharton community about the different areas and functions within the health care community, provide a social outlet for those interested in health care, and assist Wharton community members seeking health care-related careers.

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Wharton Healthcare International Volunteer Project

WHIVP is designed to give Wharton Health Care Management students the opportunity to participate in service projects for health care systems with limited resources and severe health problems such as HIV. WHIVP trips are student-organized, student-run, and student-led. Projects give participants exposure to health care challenges in the developing world as well as the opportunity to work closely with organizations on the ground to develop viable strategies to improve their operations. Projects typically take place during winter break (late December to early January) and summer break (end of August) but depend on the individual project details. Each year, small groups of students volunteer for two to three week consulting engagements worldwide. In the past, students have worked with the Wharton Health Care Management Alumni Association in South Africa with the City of Cape Town Health System. In the winter of 2004, a team traveled to India to create an HIV epidemiologic profile and improve HIV screening and data collection for the Andhra Pradesh State AIDS Control Society. In the summer of 2005, a team spent several weeks working with an HIV and family health clinic in Gaborone, Botswana to provide a financial and operational assessment of the clinic. This past winter, students developed a metrics and reporting structure for Aravind Eye Hospitals to manage future expansion of its operations from its current base in Tami Nadu, India.

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Wharton Health Care Management Program

The Wharton School's MBA in Health Care Management is a full-time, two-year program that combines the core MBA requirements with an interdisciplinary health care major. Students thus gain the full range of managerial and technical expertise as well as addressing comprehensively the complex and multi-faceted aspects of the US health care system. The Program's graduates are exceptionally well prepared to play leading roles in the diverse organizations and specialties that make up this vitally important industry, one that is constantly changing as a result of innovations in science and technology, economic forces, human demand, and government and social policy. Alumni have established careers in pharmaceutical and medical product companies, financial services, hospitals and other medical institutions, entrepreneurial ventures, consulting firms, foundations, industry, and government-many of them holding positions as chief executive officers, directors, and other key decision makers.

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Acknowledgments

Eduardo Cisneros WG '07
The Challenges That Remain - Lee E. Babiss, PhD

Brian C. DeSchuytner WG '06
The Beginning of a New Era in Medicine - Stan Bernard, MD, MBA
The End of Trial and Error - Mara G. Aspinall, MBA

Janhavi Kirtane Nene WG '07
Into the 21st Century of Health Care - Newt Gingrich
Taming TennCare - Phil Bredesen

Tamiza Parpia, PhD WG '07
A Total Framework for Corporate Citizenship - Hank A. McKinnell, PhD
Regulating the Transformation - Lawrence J. Lesko, PhD

Anil Saggi WG '07
India's Move Towards Innovation - G.V. Prasad
WHIVP 2005: Aravind Eye Hospitals
Health Care Systems of the Future - John R. Kimberly, PhD