

# The 'biomedical ecosystem'

*delivering better health and prosperity*

The overall message is simple: biomedical innovation – and the public policies and new technologies that sustain and advance innovation – are crucial to the future of biomedical science and the health and well being of our society. In fact, I believe innovation leading to new diagnostics and therapeutics is the **ONLY** answer to our healthcare problems, from treating the scourge of the disease to reducing related costs. But while the message is simple, the challenges, of course, are complex.

**By Dr Peter B. Corr**

**O**ne way to meet these challenges head-on is for all of us in the biomedical community to work together more effectively than ever before. If we look to the recent past, we can see that we have been particularly successful when we collaborate in an environment that encourages innovation.

Just look at the dramatic decrease in mortality over the last several decades in key areas of disease: rheumatic heart disease, 83%; atherosclerosis, 74%; ulcers, 72%; ischaemic heart disease, 62%; emphysema, 57% and hypertension, 21%.

As a result of these and many other advances, people are living longer. Average life expectancy at birth in Europe has risen by 11 years from 1950 to 2000. According to the United Nations, the average life expectancy in the EU-15 in 2000 was 81.5 years for females and 74.9 years for males. By 2050 well over half of all adults in Europe will be at least 65 years of age. The number of people over 80 in the EU 25 will rise from 18.8 million today to 34.7 million in 2030. And today, the number of

Americans estimated to be 100 years old or older – 71,000 – is expected to balloon by more than three-fold to 241,000 by 2020.

Clearly, medicines play a significant role, providing better treatment for a variety of serious medical problems. Over the past 40 years, the use of medicines has helped reduce the number of hospital admissions in the UK by half for 12 major diseases (*ABPI, 2004*). The same is true in the US.

And, of course, we know that staying out of hospital lowers total healthcare costs considerably. For example, cholesterol-lowering medicines at a cost of less than €3 a day can help patients avoid coronary bypass surgery at a cost of tens of thousands of euros (*EFPIA, 2004*).

Many people also do not realise that medicines in the US still account for only about 10% of the total \$1.9 trillion spent on healthcare – about the same percentage as in the 1960s – even as today's medicines do more of the 'heavy lifting' to keep people out of hospitals and other healthcare facilities. In short: medicines save lives and money.

### Redirecting the debate

There's an old Chinese proverb – a curse actually – that applies to the world of healthcare today. 'May you live in interesting times!' These certainly ARE interesting times.

On the one hand, in a tough business environment, all we hear about is the rising cost of healthcare – a problem especially targeted to our industry. On the other hand, there are enormous opportunities to discover and develop innovative medicines that will help people lead healthier, more productive lives while saving costs in the long run.

One reason for this dichotomy is that few people understand our most fundamental asset – the true value of our science. And fewer understand what we actually do as a biomedical community.

So, in addition to our scientific collaborations, we must come together as an industry – as stewards of science – to educate people on the value of medicines, the value of our science, and the benefit/risk model of our research and development process. We simply cannot develop mutually beneficial opportunities if we are under siege and the value of innovative therapeutics is not understood relative to other healthcare costs.

Again, our track record tells us that the best ways to control costs will be to improve care, not to ration it.

Kevin Murphy and Robert Topel, two economists at the University of Chicago, analysed data in the US and came up with some interesting facts. They found that even modest reductions in death rates due to common killers could produce literally trillions of dollars in added economic value to society for affected individuals over their lifetime. This economic value is based on improvements in life expectancy, productivity and income, among other variables.

Just a 10% reduction in deaths from cancers, for example, would pay off in more than \$4 trillion in overall economic value to society during the lifespan of Americans living today. A 10% reduction in deaths from diabetes would generate more than \$450 billion in similar economic gains.

According to the World Health Organisation, increasing life expectancy at birth by 10% will increase the economic growth rate in Europe by 0.35% a year. Conversely, the EU still loses more than €100 billion with the direct and indirect costs of respiratory diseases and €135 billion to cardiovascular diseases, including 8 million disability adjusted life years lost. The cost of mental health alone is estimated at 3% to 4% of GDP.

We also know that investments in R&D con-

| Economic Value of Health to Society    |  |
|--|--|
| Cause of Death                         | Impact of 10% Decrease (Billions of Dollars) |
| Major Cardiovascular Diseases          | \$5,142                                      |
| Malignant Neoplasms                    | 4,359  |
| Infectious Diseases (including AIDS)   | 644  |
| Chronic Obstructive Pulmonary Diseases | 605  |
| Pneumonia and Influenza                | 358  |
| Diabetes                               | 449  |
| Chronic Liver Disease and Cirrhosis    | 310  |
| Accidents and Adverse Effects          | 1,369  |
| Homicide and Legal Intervention        | 413  |
| Suicide                                | 508  |
| Other                                  | 3,006  |
| <b>All Causes</b>                      | <b>\$17,163</b>                              |

tribute to our economic competitiveness. According to a report from the National Innovation Initiative of the Council on Competitiveness: "Innovation will be the single most important factor in determining America's success through the 21st century."

That is why we believe that healthcare regulators and governments should begin to focus on reducing the overall cost burden of disease rather than just the cost of the therapies that treat or prevent disease.

### From sickcare to healthcare

Albert Einstein once said that the definition of insanity is doing the same thing over and over and expecting a different result. As we look for ways to reduce the burden of disease in our complex world, we simply cannot continue doing the same things over and over. We need to change the healthcare paradigm – from a focus on triage in late-stage diseases to prevention, early diagnosis and targeted treatment.

If we work together to accelerate this shift from 'sickcare' to healthcare – which will include a much more empowered healthcare consumer – we will become a healthier and more prosperous society. The key to wellness, then, will be to focus on: 1) prevention; 2) better diagnostics; 3) earlier and more focused treatment; and 4) improved compliance on the part of patients.

● **Focus on prevention** – As providers and consumers, we must have a better understanding of disease and how to remain healthy. Currently there are no adequate incentives encouraging people to

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make healthy lifestyle choices to help prevent illness. We must also make sure consumers have access to healthcare, as well as accurate information, so they can make the right decisions.

- **Earlier and better diagnostics** – Diagnostic technologies are improving faster than the development of new medicines, with greater sensitivity and specificity. With earlier and better diagnoses, we can treat or cure many diseases before they become more acute ...and expensive.

- **Earlier, more focused treatment** – We are on the cusp of innovative treatments for many major diseases. With the emergence of pharmacogenomics and other new disciplines, we are also able to focus on higher-risk populations and develop novel approaches to treating disease. Through such innovations in medicine, many cancers and cardiovascular disease, for example, can become managed conditions, not killers. The result will be a healthier ageing society.

- **Improved compliance** – Better patient compliance to prescribed therapies would save millions of lives and billions of dollars in healthcare costs. That is why our healthcare system should offer incentives to encourage healthier behaviour, including better compliance to prescribed therapies. Without consistent compliance to therapies, the totality of benefits (including financial) cannot be realised.

In some of the most significant chronic conditions (high cholesterol, high blood pressure and diabetes), about of half of patients today between

the ages of 25 and 64 stop taking their medications after 18 months (*source: Integrated Health Information Services, Inc*). In addition to incentives, we can help increase compliance with improved drug delivery systems, so medicines are easier to take or can be taken less frequently.

### The challenges of R&D

Despite the best of intentions, the process of discovering, developing and introducing effective medicines for patients in need is an enormous challenge. A potential therapeutic must travel a long and exhaustive journey through research, pre-clinical development, increasingly expensive clinical trials and regulatory approval.

After an average of 12 to 15 years and nearly a billion dollars, if all goes well, that new medicine may end up helping patients.

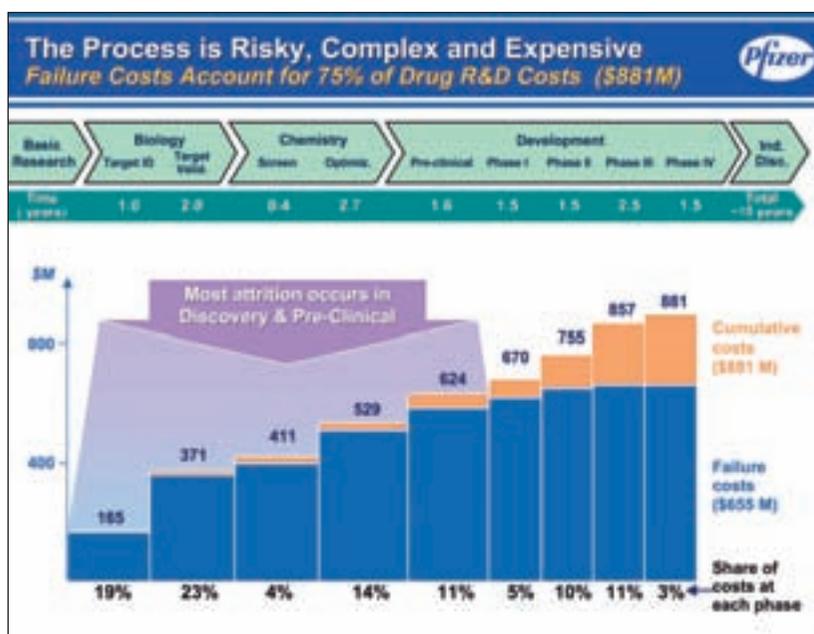
Perhaps the biggest challenges are the high failure rates and attrition in R&D, which drive up costs. Much of the cost in discovery, in particular, comes from failures. While we always learn from failures, the resulting attrition accounts for 75% of the cost of R&D for new chemical entities (*source: Boston Consulting Group*).

Even when we succeed, only one in three medicines generates a return sufficient to cover its investment. This is why the so-called 'blockbuster' drugs have been essential for our survival – they must support the entire portfolio, including those medicines that are never able to re-coup their R&D investment.

In 2004, global R&D expenditures on ethical pharmaceuticals reached \$53 billion. Now the figure is closer to \$60 billion. Over the past 10 years, global R&D expenditures have grown by more than 70% (*source: CMR International Ltd. 2004 R&D Factbook*).

Despite these rising costs, there is some good news – the total number of drug launches, including biologics and vaccines, has increased. Between 1995 and 2004, the total number of drugs launched was the highest in all of the 10-year intervals since 1945, though approvals for 2003, 2004 and particularly 2005 were disappointing (in 2005 the FDA approved only 18 new molecular entities).

So higher rates of attrition, increased regulatory demands and a focus on unprecedented targets have led to higher costs and lower efficiency – but not a decline in innovation. Today's scientists are as, if not more, innovative than ever before. Even if we must deal with the very real challenges of higher costs and increasing regulatory demands, our understanding of disease processes, coupled with new and vastly improved clinical technologies, will



ultimately enhance the output of new therapies, hopefully in the near term.

### Safety first

All of these challenges, of course, must also be met within the broad context of patient safety. Simply put, the pursuit of innovative medicines AND safety must go hand in hand.

Here to, there are significant challenges, including distrust for our industry and a lack of understanding about benefit/risk. Overall, safety cannot be defined only by risk, but by the balance between benefit and risk – a balance, incidentally, that we consider for all the choices we make in life. The key question is this: Are we better off with a new medicine and its inherent risk than not having the medicine at all?

To ensure the highest possible degree of safety in the development and use of innovative medicines, the biomedical industry needs regulatory standardisation to help us deal with the increasing complexities of regulation, a regulatory infrastructure to support the avalanche of scientific and technological advances, and perhaps most important, better communication.

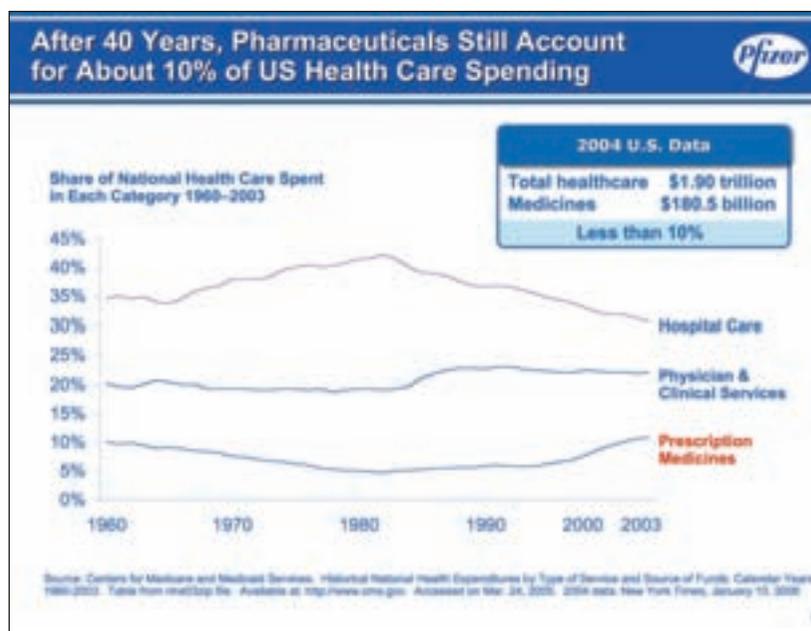
As far as Pfizer is concerned, the safety issue is clear: we are in the business of making products for health, so we have a moral imperative to protect the health of the public. Putting safety first is both common sense and good business. If patients and physicians do not think we work very hard to make drugs as safe as possible, then they will go elsewhere.

Don't forget we are patients too. We, and our families, rely on the same medicines as everyone else. So, there must be a balance between our concerns about safety and the need for biomedical innovation that will provide the important, new medicines that patients desperately need.

### Meeting the challenges head on

Three indispensable elements will help meet all these challenges.

- **Increased R&D productivity** – discovering, testing and developing new therapies on a scale and with efficiencies that can meet the global burden of disease. Simply put, we must reduce the attrition rate in the pipeline – more compounds moving from discovery to development must survive the process and end up as significant, approved therapies that meet medical needs.
- **Alliances and agreements with biotechnology firms, academia and public research organisations** – to maximise the resources of the biomedical community and advance basic science.



- **Public policies and incentives that advance innovation** – including regulatory efficiencies and regulatory harmonisation across the globe. Critical intellectual property protections are also essential.

Increasing productivity is key. We must modify attrition rates and develop faster processes to determine the efficacy and safety of compounds earlier in the process, before we invest too much time and too many resources. If we can do this, we can increase the yield in discovery, improve the quality of our early development candidates and balance risk in our development portfolios.

This is one area where partnerships can have a huge impact. Believe me, partnerships are not just a feel-good idea. They are essential for preserving and strengthening the delicate 'biomedical ecosystem' that already exists, which has created unparalleled advances in science and medicine over the past several decades.

While we must avoid even the appearance of conflicts of interest among academia, government and industry, we can strengthen these natural links – and we must. Clearly, the biomedical industry provides a significant share of funding and drives the R&D process, from discovery of new therapies to development and ultimately to market.

Given the complexities, risk and expense, we can accomplish much more, with less cost and duplication of effort, when a variety of institutions and organisations bring their special strengths to bear.

Pfizer's R&D budget will be about \$7.8 billion in 2006. This is about 15% of what is spent

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worldwide by the private-sector pharmaceutical-biotechnology community. Therefore, 85% of the ideas churning in our community are external to Pfizer, so we must be outwardly focused.

In this spirit of partnership we also need support from other sectors to fuel innovation. This support includes:

- **Successful healthcare systems** – efficient delivery and distribution of services and efficient pricing and reimbursement for those services.
- **An effective use of intellectual property** – including enforcement of IP rights so that the enormous investments in discovery and development will continue.
- **Adequate and predictable regulatory requirements** – including a safe, efficient and transparent medicine approval process, with post-marketing studies, global harmonisation of regulations, and adjustments in regulatory requirements that reflect advances in science and technology.

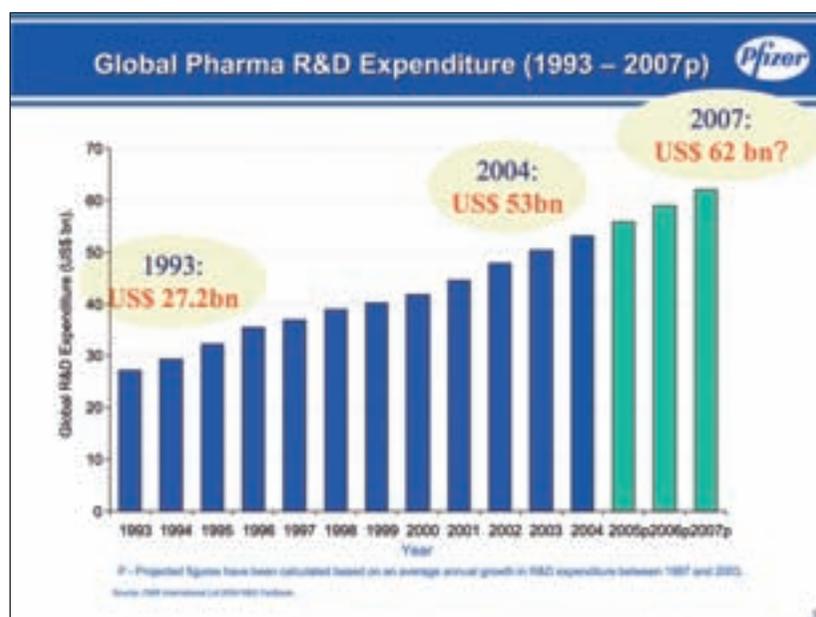
With a quantitative framework to inform the drug approval process, and with changes apparent at all stages, regulators and industry can align on benefits and risks, agree on the process itself, and agree on required data and plans for data collection – before New Drug Applications (NDAs) are submitted, during approval and in post-approval studies.

Many of us in industry, working through committees of the Pharmaceutical Research and Manufacturers Association of America (PhRMA) and The European Federation of Pharmaceutical

Industries and Associations (EFPIA) Innovative Medicines Initiative, among others, have been collaborating in recent years with the FDA, NIH, AAMC and other bodies to begin addressing some of these issues in a pre-competitive manner, with a focus on improving industry productivity and efficiency.

### Let me focus on four initiatives

- **Biomarkers consortium** – facilitating drug development by working with the FDA, NIH and others to establish evidence in early trials that a drug can reach its target and modify that target in some positive way; identify early markers for organ toxicity that can better define safety issues; identify criteria for dose selection for Phase III clinical trials; and ultimately provide new surrogate markers as endpoints for regulatory approval.
- **Novel adaptive trial designs** – leading to better treatment of trial participants, more efficient use of resources, and more rapid progress at less cost. Poor clinical trial design, poor understanding of dose response, and lack of drug efficacy are common reasons why 30-50% of Phase III trials fail to produce marketable therapies. Discussions around trial designs cover improved planning for safety, minimising data collection requirements, and enhancing the use of technology and data management tools to improve efficiency, as well as sample size, treatment allocation ratios, dose and treatment arms, adapting hypotheses, patient entry criteria, observational schemes, and test statistics.
- **Predictive models for safety and efficacy** – addressing the predictability of various tools and their use to reduce compound attrition. The initial focus will be on efficacy models for both pre-clinical and clinical stages, safety and toxicology and compound properties.
- **Exploratory Investigational New Drugs (IND)** – a risk-based testing approach for early compound selection and therapeutic screening in humans. The Exploratory IND is intended to investigate pharmacologic and pharmacokinetic endpoints in a way that provides answers to specific questions while minimising drug substance requirements. The key objectives are to test multiple new molecular entities (NMEs) or formulations in one clinical trial under a single administrative procedure; identify or confirm new therapeutic targets with limited risk; obtain human PK and PD earlier at minimal patient risk; select better compounds or formulations with less of a chance of failure in later clinical development; reduce development



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times and direct resources to more productive activities; and design safer, more effective dosage regimens earlier.

Through these initiatives and many others, we are trying to create an environment in which scientific and technological innovation can flourish, so we can advance health and healthcare overall and develop effective therapeutics for patients in need, both in the developed and developing worlds. Such collaborations – the cornerstone of the scientific process – are essential for overcoming the enormously complex challenges we face.

If researchers can develop a remote control-sized device to analyse human DNA using micro-fabrication methods, which they have... And if complex computer models can be used to test new pharmaceutical treatments virtually, which they are... Then we are certainly capable of coming together to improve R&D efficiency and productivity – to truly realise the promise of the biomedical endeavour – for the health and well being of everyone.

Let me bring the importance of this discussion closer to home. Many of us will reach the age of 85, and about half of us will develop Alzheimer's disease. Today, there are effective palliative therapies, but nothing stops the progression of the disease. So left unchecked we will require institutionalisation and expensive round-the-clock supervision.

But there is an alternative.

We must invest in the science and technology that lead to the innovative therapeutics that will keep us mentally alert, independent and out of such facilities. It is a huge challenge, but we have met similar challenges before, and we can do it again, together.

I am convinced that advances in biomedical research will yield effective treatments and will improve medical outcomes and lower medical costs.

If we are to realise these advances, however, the institutions that form the biomedical ecosystem, from academic centres, national laboratories and the biomedical industry to regulatory agencies, must be maintained and strengthened – and they must be encouraged to work collaboratively in the pursuit of scientific and biomedical innovation.

Thomas Edison said it simply: "There's a way to do it better...find it!" Let's work together and find the better way to advance science and improve health.

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