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STATEMENT OF

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"TECHNOLOGY AND INNOVATION: THEIR EFFECTS ON COST GROWTH OF HEALTHCARE"

BEFORE THE

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INTRODUCTION

Good morning Mr. Chairman and Members of the Committee. I am Dr. Mark B. McClellan, Commissioner of Food and Drugs, and I welcome this opportunity to testify before the Committee today. As we enter the 21st century, America leads the world in developing and commercializing new medical innovations and technologies. From information technology to biotechnology to materials science, United States (U.S.) scientists and high technology workers are making new discoveries and developing new products every day that are steadily improving the quality of our lives. This progress is critical to our health and our economic prosperity.

Innovations resulting from breakthroughs in science and technology fuel economic growth. According to the Department of Commerce, the information technology sector accounts for just seven percent of all businesses in the U.S. economy, yet between 1996 and 2000, it drove 28 percent of the overall U.S. real economic growth and created jobs at twice the pace of other sectors. These jobs paid twice as much on average as well. Many leading economists now believe that new discoveries in information technology led to investments over the last couple of decades that helped account for the historic surge in economy-wide productivity growth in the 1990s.

BACKGROUND

While all economists appreciate the contribution of such economic growth to the well-being of the U.S., there is often less appreciation of the contribution of innovations in biomedical technology. A primary reason is that technological change in medicine brings benefits in addition to direct economic gains, including increased longevity, improved quality of life, and less time absent from work. These benefits are not taken into account in standard measures of

aggregate economic output. If a country had real gains in its overall health, but not in its material well being (most often measured by per-capita income) the national income accounts would not change, even though those accounts are often thought to measure the well being of a population.[i] In addition, the direct economic and public health benefits of developing important new medicines often takes considerable time to be realized. If a high-technology firm invents a better memory chip, the time to get that innovation into products sold in the U.S. could potentially be as short as a matter of weeks or months. Regardless of how promising a drug or other new treatment appears in the laboratory or even in animals, it must undergo extensive clinical trials before it can be approved as safe and effective for market introduction.

In recent years, economists have tried to quantify the value of biomedical innovation to society. Some economists actually estimate that the value of the longer and better lives that have resulted from translating new biomedical knowledge into steps to prevent and slow diseases is worth literally many trillions of dollars in better health. In particular, the value of biomedical innovation to the U.S. equals the value of innovation in all other sectors of the American economy combined.[ii] Even with the benefits of new medical technology, the fact remains that technological innovation is a major source of increase in real per-capita medical spending in the U.S. Innovations in medicine can reduce spending on medical care. For example, treatments ranging from effective care for depression to laser eye surgery are much less expensive than in years past. But many new technologies result in increased costs, and in some instances the net effect of overall technological change has been to raise health care expenditures. First, when a treatment becomes less expensive and safer (fewer complications), more patients may decide that a treatment is worth the risks and unpleasantness. In the early 1980s, relatively few seniors had cataracts removed because the procedure required an unpleasant hospital stay, often had

complications, and yielded imperfect results. Today, thanks to improvements in technology, millions more seniors with more modest visual impairment find that modern cataract surgery improves their lives. Second, many treatments exist that do things that simply were not possible before, such as allowing many patients to survive previously fatal or impairing diseases. Americans spend much more on transportation today than they did a century ago because of innovations in transportation ranging from automobiles and airplanes, allow people to go places they simply could not before. Similarly, patients with heart disease, cerebrovascular disease, cancer, arthritis, AIDS, and countless other conditions are living longer and better lives because of medical innovations that transformed fatal illnesses or illnesses that could only be treated with comfort measures into manageable conditions.

The increased spending on health care does not necessarily reflect negatively on technological change. While many studies attribute a large share of the age- and price-adjusted growth in per capita medical spending in recent decades to technological innovation, a key issue is whether the benefits of innovation are rising faster or slower than the costs.

This important question is difficult to answer. It depends on our ability to determine the value of output from the health services sector, and putting a value on a longer life or a higher quality of life is hard to appraise. Nonetheless, a limited number of studies have attempted to aggregate the medical value of new innovations across the whole health care economy in general and the drug industry in particular. Even with these studies, it can be difficult to sort out whether the observed improvements in health are from medical technology, or from other factors that may influence health outcomes, such as higher incomes, improved public health measures, or changes in behavior as a result of greater biomedical knowledge. To try to identify the net value of

medical technology itself, several studies have attempted to measure the value of specific kinds of innovations. A number of studies have examined outcomes for specific illnesses, such as heart attacks and depression, where the impact of specific changes in technology can be examined more closely. While none of these studies are completely convincing in themselves, they consistently show that medical innovation has greatly increased value, that is, the value of the improved health is far larger than the increase in spending.[iii]

The reasons are quite intuitive. Individuals are living longer and better lives, because our nation is making real progress in the quality of medical care for many conditions. While the achievements of health improvements in past decades have been impressive, recent progress in genomics, proteomics, nanotechnology, information technology, and many other fields promise even greater improvements in our lives in the years ahead.

We achieved the improvements of the last few decades without a sophisticated science of genomics – the human genome was sequenced in just the last few years. Genomically-based drugs, and gene and tissue therapies based on genomic sciences, are making up a growing number of the new drugs entering clinical trials. We also achieved our recent progress without the new science of proteomics, and an increasingly sophisticated understanding of how gene and protein expression interact to cause disease in individual patients. We also did it without a new generation of increasingly powerful biomedical tools based on the latest information technology that can enable sophisticated systems for supporting effective medical decision-making. These additional tools increase the future potential for more effective, more targeted, even individualized medical treatments that can cure or at least slow or halt disease progression.

IMPACT ON HEALTH CARE COSTS

As health care costs have gone up, it is increasingly important to make sure we are realizing the full value of the new medical technologies that we create. Maximizing our public health gains and our economic gains from new medical technology also requires that we encourage high value innovations and also realize more value from the products that we use. This is important for the future, because while the cost of new medical technologies may continue to rise, the potential benefits of new treatments could grow even more dramatically.

We must find better ways to increase value, to keep modern care affordable, while still encouraging medical innovation. With these unprecedented technological achievements have also come unprecedented concerns about the total spending on healthcare and, in particular, about the rising spending on these new medical technologies. Many worry that, even if these new technologies come along, they will not benefit because they will not be able to afford the high cost. While we need to take new steps to address the problem of health care affordability, we need to do it carefully. We must address this issue in a way that will not risk the tremendous potential for public health and economic benefits from continuing medical innovation by putting significant new limits on the payments or the intellectual property protections of innovative treatments that have made it through an increasingly long and costly development process.

The trade-off between maximizing the welfare of consumers today and promoting the future flow of new drugs is at the heart of most policy debates regarding pharmaceuticals. Policies aimed to lower drug prices – mandating drug discounts and controlling prices, for example – are worth pursuing only if the immediate benefit from lowering process and making drugs more widely available today compensates for the harm from reducing the future flow of new products.

It is not clear that this tradeoff is possible, or desirable. There is considerable evidence that policy choices that put at risk the incentive for drug developers to invest in new medical technology ultimately impair the public health by seeking short-term savings at the expense of higher monetary and personal costs of disease in the future through the removal of required incentives for the development of improved treatments.

In particular, there is concern about the threats to innovation because the process of medical innovation – of turning sound ideas from insights in the biomedical laboratory sciences into safe and effective products for treatments – has steadily become more costly. Getting a product into general use is an increasingly lengthy and costly business and fraught with significant risk.[iv] Some estimates put the total cost of developing a novel drug at more than $800 million.[v] Too often, the process is unpredictable, and may take years of hard work with high costs for product testing and developing reliable production lines.[vi]

Many people involved in the development of new medical technology believe the slowdown in drug approvals is likely to be only temporary. Currently, the National Institutes of Health (NIH) is completing a five-year doubling of its budget, to more than $27 billion. Less well known is that spending on research and development by pharmaceutical companies worldwide has also doubled since 1995 and now is estimated to be more than $54 billion. The impact of these investments in research is already becoming evident in the form of more investigational new drugs (INDs) under development than ever.

But if the impact of information technology on the economy is any guide, it may require a decade or more of increased investments in order to have a real impact on productivity - on how

much output we get as a result of these inputs. And it could take much longer, because of the unusual length and uncertainty of the product development process in health care. At this point in genomics, for example, scientists are still primarily gathering information, sorting out patterns, and only starting to understand what the turning on or off of hundreds of genes by a new drug means for whether it is safe and effective in patients. The increase in the time and cost of product development has already been associated with a decline in the number of truly new drugs and biological treatments being approved by FDA. Last year, FDA approved 21 new molecular entities (the truly new drugs) down from 44 such entities in 1996. And FDA approved 12 new biological license applications (BLAs), down from 27 BLAs in 1998. The decline in products approved is not the result of FDA rejecting more applications; it is directly related to a decline in the number of new applications for drugs and biologics coming in to the Agency, and it is a worldwide phenomenon.[vii]

TRADITIONAL APPROACHES VERSUS NEW TECHNOLOGIES

While there are and no doubt will continue to be traditional "blockbuster"-type drugs in development that may bring important public health benefits to many millions of patients, breakthroughs in genomics, proteomics, and other new fields of molecular biology also hold great promise for truly individualized drug therapy in which diagnostic tests and novel drug delivery mechanisms guide the use of medications, turning heterogeneous diseases like cancer and heart disease into distinct types of pathologies that appropriately require distinct therapeutic approaches. Other new technologies are breaking down the traditional barriers between drugs, tissues, and devices, including products in development that are combinations.

Translating the new biomedical sciences into these new kinds of treatments for patients requires major new investments, and it seems plausible that such investments may take many years to reach fruition. It should not be surprising that we haven't yet seen the huge increase in biomedical investment of the past decade, and especially the last few years, turn into more and more valuable medical products for patients. But the fact remains that developers of biomedical products are not producing drugs particularly faster than they were before all these innovations came along. From a public health standpoint, with millions of Americans suffering from diseases that may be curable or at least manageable in the not too distant future, we cannot afford to wait many more years for all these investments to become valuable products.

On the research and development side, it's possible that the costs and uncertainty of developing new treatments could keep rising. It's easy to see how this could happen: there are not many more obvious drug targets left to exploit, and developing genomics- and proteomics-based therapies remains very costly. So far, genomics has mainly added steps at the front end of the development process, through microarray testing of gene responses, and has not reduced the costs of clinical research significantly. On the policy side, there is intense pressure to make health care more affordable, and so the focus tends to be on reducing shorter term medical costs.

POTENTIAL POLICY SOLUTIONS

We can take steps today to improve the development and use of medical technologies, and find creative policy solutions that both support innovation and make healthcare more affordable, particularly for those with limited means and great needs. There are many ways to do this, but above all, we need to increase value in the process of developing and using new medical technologies. To these ends, a key element of FDA's new strategic action plan is efficient risk management. In all of FDA's major policies and regulations, the Agency is seeking to use the

best biomedical science, the best risk management science, and the best economic science to achieve its health policy goals as efficiently as possible.

The enormous growth in research investment has required the Agency to deal with more complex and innovative products in development than ever before. As discoveries made in the laboratory are flowing into the medical products consumers are using, it means that the Agency is challenged to upgrade its own science to keep pace with this new innovation and the growing sophistication of manufactures. As part of a new FDA initiative on improving medical innovation announced in January 2003, the FDA is taking specific steps to help foster more efficient innovation, especially in emerging areas or those of great medical need. The initiative has several elements that are described below.

- **Need for Performance Measures**

One element of this plan is the development of "quality systems" for the Agency's review procedures. The idea is to build on FDA's professional staff expertise to identify and apply best management practices internally to the review processes. This includes using peer review programs coupled with more empirical data for drug and device reviewers to exchange ideas and use each other's experience to learn about best practices. A key part of this effort is developing performance measures that the Agency's experts believe are related to the goal of approving safe and effective treatments as efficiently as possible.

FDA is also working to develop new guidance documents that can bring more predictability to regulatory process. These are in a tradition of FDA documents that serve as roadmaps for drug and device developers, offering guidance on how to structure studies to prove that new

treatments work. These new documents represent an enhanced effort to combine internal expertise with input from outside experts to make sure that are regulatory methods are up to date in important areas of technology development. Some of the guidance will focus specifically on diabetes, obesity, and cancer. Despite all the innovation that has already occurred, these are therapeutic areas that remain underserved by effective treatments and that have promising technologies under development today.

- **Developing New Guidance for New Areas**

The Agency is also developing guidance in new areas of technology development, including pharmacogenomics, novel drug delivery systems, and cell and gene therapy. In each of these cases, the Agency expects to learn something from outside experts in the open process of developing them. For example, FDA is setting up a "research exemption" program for product developers as well as academic experts to share data on pharmacogenomic results, such as microarray studies, that may be useful for predicting clinical benefits and risks and thus reducing the costs of demonstrating safety and effectiveness. This kind of information can also be used to increase the value of a new medicine by allowing doctors to target drugs to patients most likely to derive a clinical benefit or least likely to suffer a rare side effect. The goal in all of these endeavors is to use the new regulatory standards to reduce the time and cost of product development and to ensure that the Agency's regulatory procedures are current at the same time. We hope this will lead to earlier and broader access to new treatments.

- **Rapid Access to Generic Drugs**

Supporting the development of safe and effective new treatments is one of the most important ways that FDA can promote the public health. But when appropriate patents have expired, we

need to facilitate broader access through lower-cost generic drug alternatives. Generic drug manufacturers produce medications that are just as safe and effective as their brand counterparts. Yet the prices of generics are generally much lower. A generic version of a $72 average brand-name prescription costs about $17. With more brand-name medications coming off patent - more than 200 of them in the next few years - and with ever-improving scientific knowledge and public awareness about the benefits of generic drugs, the health and economic benefits of using generic drugs are constantly growing.

Encouraging rapid and fair access to more affordable generic medications is one of FDA's major priorities. FDA is proposing new resources to enable us to implement major reforms in its generic drug programs to reduce the time it takes to get a generic drug approved. Right now, it takes well over a year and a half on average to approve a new generic medication and we think we can significantly improve. In addition, the Agency recently finalized a generic drug final rule that would expedite and increase access to more affordable generic drugs by limiting the ability of innovator drug companies to receive multiple extensions that delay entry of generic competition. This final rule is projected to save American consumers $35 billion dollars over the next 10 years. Furthermore, this rule makes changes to the patent listing process that are also designed to improve generic competition.

- **Revised Good Manufacturing Practices**

Another application of the principle of efficient risk management to reduce medical costs and improved outcomes is in improving the way that medical products are manufactured. These guidelines are referred to as good manufacturing practices (GMPs), and these GMP regulations for drugs have not been updated in 25 years. Meanwhile, best practices in manufacturing

technologies and methods have undergone significant progress over that time, particularly in other high-tech industries. For example, the semiconductor industry also has a very low tolerance for impurities and inaccuracies in production. When its production processes were lagging because of high costs and too many errors that industry helped invent the "six sigma" production methods. Through continuous quality improvement, those methods achieved enormous improvements in production cost and quality, and they have since been widely adopted in manufacturing industries.

But continuous quality improvement in manufacturing hasn't been the subject of as much attention in the pharmaceutical industry, even though many experts on manufacturing processes believe that large savings in production costs could be realized while maintaining very high standards for purity and accuracy. FDA wants to make sure that regulations are encouraging such progress, not standing in the way. The Agency is working on a program for developing new GMPs based on the latest science of risk management and quality assurance. The new standards would be designed to encourage cost-reducing and precision-enhancing innovation in manufacturing and technology, and to ensure that all three FDA medical centers use consistent and up-to-date methods, including inspectors specializing in particular types of production methods.

In addition to substantial savings in the development and manufacturing of safe and effective medical products, there are many more opportunities to increase the value of the medical products FDA regulates after they are approved and maximize their public health benefits. By making better information available to patients and doctors about the benefits and side effects of

new medical technologies, people can realize more value from these products by making better decisions about when to utilize them for maximum advantage.

- **Prevention of Medical Errors**

Approved medical products, while safe and effective when used as intended, can be involved in costly and potentially preventable adverse events, including medical errors. A November 1999 report of the Institute of Medicine (IOM), entitled "To Err Is Human: Building a Safer Health System," focused a great deal of attention on the issue of medical errors and patient safety. The report indicated that as many as 44,000 to 98,000 people die in hospitals each year as the result of medical errors. Even using the lower estimate, this would make medical errors the eighth leading cause of death in this country. About 7,000 people per year are estimated to die from medication errors alone—about 16 percent more deaths than the number attributable to work-related injuries.[viii]

Preventable errors and complications involving prescription drugs alone are also responsible for billions of dollars in additional health care costs each year, in addition to all of the unnecessary suffering. The IOM report estimates that medical errors cost the Nation about $37.6 billion each year; about $17 billion of those costs are associated with preventable errors. About half of the expenditures for preventable medical errors are for direct health care costs. That's too much money that would be better spent on proper care.

FDA has a role in helping to avoid these costly errors by supporting the development and use of safer health care systems; systems that help health professionals avoid errors and deliver higher quality care. The majority of medical errors do not result from individual recklessness, the

report says, but from basic flaws in the way the health system is organized. Stocking patient-care units in hospitals, for example, with certain full-strength drugs (even though they are toxic unless diluted) has resulted in deadly mistakes. And illegible writing in medical records has resulted in administration of a drug for which the patient has a known allergy.

To help mitigate these risks, earlier this year FDA proposed a universal bar coding system for prescription medications and blood products. Coupled with barcode readers and electronic medical records, bar codes on drugs are expected to reduce the rate of medication errors that occur at the stage of dispensing and administering medications by half or more. Bar codes can help make sure that the right patient gets the right medication in the right dose at the right time, and soon a standardized system of codes will be built in to all drug packaging. Based on the published relationships between hospital admissions and adverse drug events, FDA has estimated that of 372,000 preventable adverse drug events per year in hospitals, bar code identifiers on drug products could be expected to avoid about 22 percent of these events. Over 20 years, FDA expects more than 413,000 fewer adverse drug events because of bar coded products. The average annual benefit of avoiding these events is $3.9 billion dollars in patient pain and suffering and direct treatment costs.[ix] FDA's work on standards has another benefit. According to the hospital industry and many health care purchasers, standard bar codes will speed the adoption of electronic health information systems by hospitals and other healthcare organizations, because the standardized codes increase the payoff from having electronic systems.

Even with the best available data, drugs are sometimes found to have adverse effects that could not have been predicted or uncovered in any feasible clinical trial. Most of these subtle or rare

problems, such as liver toxicities, that occur in a small number of people and most become apparent only after drugs have been used in real-world patient populations for some period of time. The Agency must have effective systems in place to detect such problems, so that preventable adverse events are identified, and better ways can be found to prevent these events.

As part of this effort, the Agency is working on developing information technology tools that will allow it to link into the electronic medical records of large healthcare institutions and organizations, and automatically scan medical records for combinations of new drugs and clinical endpoints such as blood test results that might contain harbingers of trouble. The idea is to use modern information technology to acquire information on associations between adverse events and use of a medical product that might warrant focused further investigation. FDA wants to have systems in place that allow us to be proactive in collecting this clinical information, rather than continuing to rely primarily on vigilant doctors and FDA's voluntary adverse event reporting systems.

- **Safety and Efficacy Studies for Approved Medical Products**

More studies of the safety and effectiveness of medical products after they are approved can be very helpful for learning more about the risks and benefits of medications in special populations and can help guide more informed medical decisions. For example for a new cancer drug that recently gained accelerated approval, the National Cancer Institute is funding so-called "Phase 4" studies to confirm clinical benefits and help assess longer-term risks. These efforts to use modern information systems and post-approval studies can add substantially to the body of knowledge about which patients are most and least likely to benefit from an approved treatment, in turn leading to higher-value treatment decisions.

- **Better Informed Consumers**

FDA is also working to encourage more effective, high-value use of medical treatments by helping patients and health professionals get access to the latest and best information on risks and benefits. For all that improving medical technology can do, it is much less than people can do through their own choices to improve their health. From encouraging better guidance to patients in pharmacy labels, to clearer guidance on communicating risk and benefit information in direct to consumer advertising, to new enforcement initiatives against dietary supplement manufacturers who make health claims without scientific foundation, to food labeling that better discloses diet-disease information, FDA is undertaking new efforts to help consumers make better-informed decisions about how to use their health care dollars. In one recent example, FDA is working on a DailyMed program for physicians, so that a redesigned electronic product label that can be updated daily to include the most current information about a drug after they are already on the market. Only by facilitating access to complete, timely, and easily used information available to consumers and health professionals can FDA help to make sure that people are making the best decisions about their health based on the best available information.

CONCLUSION

The translation of biology into new treatments is primarily a story of the late twentieth century, and its heroes are often stubborn and straightforward scientists who plod ahead in the face of tremendous risk and uncertainty. Some of their breakthrough treatments emerge from eureka moments, but that's not the way it usually works in science. More often, new treatments result from years of meticulous plodding work to solve a countless array of complex problems in order to translate a proof of concept into a treatment that actually and reliably improves the lives of

individuals. This long and difficult process is also a delicate one that requires the right mix of incentives and safeguards to make sure people can derive the maximum benefit from safe and effective new medical technologies. Only by adopting policies that protect the incentives to develop new drugs and medical devices, and reward cost-effective medical practice and the most high value use of new technology, will we continue to realize the full benefits of these innovations. As described in this testimony, at FDA, as Commissioner of Food and Drugs, I am working to implement numerous policies, initiatives, and regulatory improvements that reflect these critical needs in order to promote increased access to high quality, safe and effective medical products, including drugs, biologics, devices and combinations of all three.

I appreciate the opportunity provided to provide this testimony and I would be pleased to respond to any questions.

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[i] "Measuring the Health of the United States Population", Brookings Papers on Economic Activity, Microeconomics, 1997, 217-272 (with Elizabeth Richardson).

[ii] Cutler, David M. and Mark McClellan. "Is technological change in medicine worth it?" *Health Affairs*; September/October 2001: 11-29.

Grabowski, H., J. Vernon, J.A. DiMasi. "Returns on research and development for 1990s new drug introductions." In "The Cost and Value of New Medicines in An Era of Change." *PharmacoEconomics* 2002;20 (Suppl 3):11-29.

[iii] Lichtenberg, Frank R. Are the Benefits of Newer Drugs Worth Their Cost? Evidence From the 1996 MEPS,"reprinted from *Health Affairs*, Vol. 20, No. 5, September/October 2001.

Kleinke, J.D. "The Price of Progress: Prescription Drugs in the Health Care Market," reprinted from *Health Affairs*, Vol. 20, No. 5, September/October 2001

Lichtenberg, Frank R. "The Effect of New Drugs on Mortality from Rare Diseases and HIV." NBER Working Paper W8677, December 2001.

[iv] DiMasi, J.A. "Uncertainty in drug development: approval success rates for new drugs" Chapter 20 in Clinical Trials and Tribulations, 2d Edition, revised and expanded. Cato AE Sutton L Cato A III, editors. New York: Marcel Dekker, 2002:361-77.

[v] DiMasi, J.A., Hansen, R.W., Grabowski, H.G. "The Price of Innovation: New Estimates of Drug Development Costs." *Journal of Health Economics*, 2003 Mar;22(2):151-85.

Kaitin KI, Ed. "Post-approval R&D raises total drug development costs to $897 million." Tufts Center for the Study of Drug Development Impact Report 2003 May/Jun;5(3)

[vi] Horrobin, David F. "Modern Biomedical Research: An Internally Self-Consistent Universe with Little Contact with Medical Reality?" *Nature Drug Discovery*; February 2003:151-154.

[vii] CDER 2002 Report to the Nation: "Improving Public Health through Human Drugs." May 13, 2003.

[viii] To Err Is Human: Building a Safer Health System. Institute of Medicine Press, 2000.

[ix] Bates, D.W., D.J. Cullen, N Laird, L.A. Peterson, S.D. Small, D Servi, et al. "Incidence of Adverse Drug Events and Potential Adverse Drug Events: Implications for Prevention. *The Journal of the American Medical Association*. July 5.1995.

Classen, D.C., S.L. Pestonik, R.S. Evans, J.F. Floyd, and J.P. Burke. 1997. "Adverse Drug Events in Hospitalized Patients: Excess Length of Stay, Extra Costs, and Attributable Mortality. *The Journal of the American Medical Association*. January 22/29.
Jha, A.K., G.J. Kuperman, J.M. Teich, L Leape, B Shea, E Rittenberg, et al. 1998. "Identifying Adverse Drug Events. *The Journal of the American Medical Association*. May.