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Chairmen Upton and Pitts, and Ranking Members Waxman and Pallone, my name is David Gollaher and I am the President and CEO of the California Healthcare Institute – CHI. I am honored to testify today on behalf of our organization, which represents some 300 biopharmaceutical and medical technology companies, along with California's leading academic medical centers and private research institutions. FDA's Prescription Drug User Fee Act (PDUFA) program has special importance to California because the biomedical industry is among our state's leading high-tech employers, directly accounting for about 270,000 jobs whose salaries average $76,000 a year. The purpose of my testimony today is to support the reauthorization of PDUFA, to underscore its critical role in drug innovation, and briefly to review a project CHI has been pursuing with the Boston Consulting Group (BCG) to gather and analyze data that accurately reflect FDA performance.

While the FDA has frequently been the target of criticism, I want to emphasize that CHI and our industry are committed to strengthening the partnership with the Agency. A strong, efficient FDA is equally important to industry and to the patients we serve. We believe that positive policy and operational improvements at the FDA, along with constructive legislation, will encourage biopharmaceutical innovation. A predictable and transparent regulatory process is an essential component of our biomedical innovation ecosystem. Since its inception, PDUFA has been a notable success. By working together, Congress, the Agency, industry and other

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stakeholders can maintain the high standards of safety and effectiveness that physicians, patients and their families expect while also enhancing the biomedical sector's ability to attract the capital essential to secure U.S. global leadership in life sciences.

1. EFFICIENT REGULATION IS ESSENTIAL TO REALIZING THE PROMISE OF ADVANCED SCIENCE

In an era of increasing global competition, the United States remains the world leader in basic biological sciences and in translating laboratory breakthroughs into new medicines for patients. Since the mid-twentieth century, America's competitive advantage in biomedical innovation has been driven by federal investment in basic research, principally through the National Institutes of Health (NIH). In the 1970s, NIH funding fueled the discovery of recombinant DNA at the University of California – San Francisco. This made possible genetic engineering and led to the creation of a whole new industry called biotechnology. More recently, in 2003, scientists at the NIH and in the private sector completed the sequencing of the human genome. The Human Genome Project took fourteen years and cost more than one billion dollars. Yet the pace of scientific advance is so rapid that today you can have your personal genome sequenced for about a thousand dollars -- a million-fold drop in price in just nine years. Low-cost human genomics has two implications. First, it enables scientists to correlate genes with diseases, and we are discovering that a great many disorders have a genetic basis. Second, it opens the way to personalized medicine, allowing physicians to determine in advance how various medicines may affect an individual. There is already a genetic test for women with breast cancer, for example, that accurately predicts whether or not a patient will respond to a targeted monoclonal antibody therapy. Only patients who test positive for a specific genetic mutation are treated with the drug.

Our expanding ability to understand diseases at the levels of genes and cells means that there has never been a time in history when the science of human health has

been so promising. Still, after a period during the 1980s and 1990s that saw the introduction of many breakthrough biotechnology drugs, along with remarkable medicines for HIV/AIDS and other infectious diseases, drug development has not kept pace with science. The reasons for this are understandable. The human body is the most complicated organism in nature, and developing drugs that have powerful effects on disease without undue side effects turns out to be extremely difficult. At the same time, faced with drug development costs that average well in excess of a billion dollars, industry is searching for the optimum model for R&D. The most productive organizational model and scale for drug research remains a quest in progress.

Beginning in the early 1980s, much of the work of translating basic scientific inventions into commercial products for patients was the province of biotechnology startups. Here the classic pattern involved a basic research discovery, say, in a university laboratory which the university patented and then licensed the invention to a company funded by venture capital. Hundreds of companies began this way, creating tens of thousands of jobs. But this model began to run into trouble after the dotcom bubble burst in 2000. The global financial crisis beginning in 2008 has further pressured venture capital, sharply reducing the reservoir of funds available for new firms. In addition, volatility in the financial markets stemming from the global contraction and European debt crisis has heightened investors' sensitivity to risk.

Risk is the necessary framework for understanding how the FDA influences drug development. Whether from the viewpoint of venture capitalists or drug company executives, regulation has always weighed as a key risk factor in decisions about capital allocation. In the drug discovery pipeline, Phase I trials are first used to evaluate if a new drug is safe, then Phase II trials are done to assess the drug's efficacy, and finally Phase III trials are performed in a larger population to confirm

the safety and efficacy of the drug. Each consecutive phase includes more people to refine the results obtained in the previous phase. Since the 1990s, the trend has shifted toward a higher and higher failure rate. The odds of drug candidates -- a new molecular entity (NME) – making it all the way through three phases of clinical trials is between five and eight percent.

Since most new drug candidates fail, in a capital-constrained environment, regulatory risk increases exponentially. As Joseph DiMasi at the Tufts Center for the Study of Drug Development observed, "Longer development times increase R&D costs and shorten the period during which drug companies can earn the returns they need to make investments financially viable. . . . longer development times reduce innovation incentives." Significantly, a study by CHI and BCG, *Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry* (February 2011), found that from the time PDUFA was first authorized in 1992 until 2007 there were clear improvements in FDA drug review performance. But comparing submissions for NMEs from 2003-2007 with 2008, there was a 28 percent increase in the number of months to approval (from an average of 14.7 months to 18.9 months). One result of longer review times at the FDA was a new drug lag, with a number of new drugs approved in Europe ahead of the U.S. from 2007-2010.

A slowdown at the FDA was frustrating to industry because it widened that gap between fresh knowledge emerging from the engine of biosciences research (much of it funded by government), on the one hand, and the application of this knowledge to human health, on the other. Meanwhile, the relationship between industry and the Agency was strained by unpredictability, by unexplained regulatory delays, by a lack of clear standards for what clinical data would ultimately be sufficient for product approval, and by a bureaucracy whose communications were inconsistent. It is worth noting that many, if not most, of industry's criticisms focused less on

matters governed by the Agency's statutory authority than on those that were the prerogatives of Agency management.

2. FDA PERFORMANCE DISPARITIES AMONG THERAPEUTIC AREAS

In 2011, there is evidence that the FDA began to address drug approval timelines. In November 2011, for example, the Agency issued a report, *Innovative Drug Approvals,* citing 35 innovative drugs that represented advances in treatment for hepatitis C, late-stage prostate cancer, lupus, drug resistant skin infections, pneumonia, and other serious disorders. This report detailed how the FDA used expedited approval authorities, flexible clinical trial requirements and resources collected under PDUFA to improve the rate of approvals. Earlier, a study from the Friends of Cancer Research noted that for oncology over the past decade, most innovative medicines were approved in the U.S. in advance of the European Union.

This is an important finding, and evidently, among therapeutic areas within the FDA, oncology is a bright spot. But recent analysis of FDA data by BCG suggests a more nuanced picture. The FDA is not a monolith; there are significant deviations in average review times, depending on a product's therapeutic area. Oncology and anti-infective drugs, for example, experience the fastest reviews, on the order of 10-15 months. For other categories – cardiovascular, central nervous system, gastro-intestinal, respiratory, etc. – average review times stretch from 20 to 30 months. As a consequence, a drug's therapeutic area influences both the time it spends under review and the probability of its being approved first in the U.S. or Europe.

It is unclear what explains differences in performance from one therapeutic area to another. Some fields may be inherently more complicated, with fewer biomarkers or with poorly understood mechanisms of action for novel drugs. Alternatively, certain therapeutic areas may be understaffed or may reflect differences in managerial priorities or effectiveness. Oncology, for example, remains a field in which there are

comparatively few effective drugs, while prevalence of cancer and public concern runs high. The same may be said of infectious diseases. Unsurprisingly, the Agency performs comparatively well in both areas.

In some ways, variations in FDA performance in different therapeutic areas suggest an opportunity. That is, the Agency is in a position to learn from its own best practices, and to replicate them across different areas. To accomplish this will require more data than we have had in the past; data that would prove equally useful for internal FDA benchmarking and for industry management.

Ideally, recognizing that the FDA must set priorities and that not all disorders pose equal threats, one would hope for basic alignment between regulation and public health. Yet, to some degree, things have gotten out of balance. Diabetes, obesity, and cardiovascular disease exert enormous, and growing, damage on health. Unfortunately, though, regulatory pathways in these areas are fraught with uncertainty. And the result is that fewer large pharmaceutical manufacturers are developing products for these indications, while venture funding for startups has all but disappeared. Within industry and the venture community alike, the common wisdom is that the Agency has, in these areas, tightened its benefit-risk calculation, demanding more data over longer periods, thus increasing the cost of clinical trials to the breaking point.

There is broad agreement between industry and the FDA about the importance of building a better shared understanding of benefits and risks. Virtually all medicines bear some capacity for harm. A zero-risk approach would shut down the development of beneficial drugs. In this regard, however, the Agency focuses almost exclusively on the *direct* risks of drugs: side effects, adverse events and so forth. These are comparatively discrete and measurable. But *indirect* risks are both difficult to observe and subject to a much longer time horizon. Where are data that

allow one to calculate the harm to public health if investors avoid an important disease because the FDA's demands for data are so extensive and its standards for drug approval so uncertain?

We are encouraged that the Agency has begun to address this challenge. Its report, *Driving Biomedical Innovation: Initiatives to Improve Products for Patients* (October, 2011), acknowledged that despite more than $95 billion invested into biomedical R&D between the NIH and industry, "these investments have not translated into a parallel increase in novel products" (p. 3). As Commissioner Margaret Hamburg's Innovation Initiative starts to unriddle the reasons for this, we hope that a top priority will be a more transparent elaboration of how the Agency manages its benefit-risk calculations, including an appreciation of indirect risk. Indeed we also acknowledge and laud PDUFA V provisions to enhance benefit-risk assessment as well as a concentration on patient-focused drug development.

3. THE IMPORTANCE OF RELIABLE DATA

A time-honored principle of management is that what gets measured gets done. We have learned a great deal in working over the past two years with BCG and the FDA, mining the Agency's data in order to gain a better understanding of how it operates, and how its performance metrics have changed over time. So we believe that there is great value in (a) regularly gathering and analyzing the best possible data; (b) updating performance metrics during the next PDUFA cycle in order to track performance consistently and longitudinally; and (c) ensuring that there is agreement among the FDA, industry, and congress that the data and how they are reported are the most accurate possible measures of agency performance. It seems ironic that for an agency that regulates more than 20 percent of American production, and depends increasingly on industry user fees, there has been so little in the way of consistent tracking mechanisms. In this vein, we believe all would

benefit from more granular information from the division review level in order to understand where things are working and where they need improvement.

4. CONCLUSION

PDUFA V represents the next step in a successful, ongoing partnership between the FDA and industry. It is important for the legislation to remain highly focused: to support the Agency in its efforts to promote biomedical innovation; to encourage it to address areas of inefficiency; to balance its imperative to protect public safety with the importance of continuing robust private-sector investment into new drugs and biologics. In the long view, public health and the economic health and competitiveness of the biomedical industry are two sides of the same coin. Without immense investment, the next generation of breakthroughs for our greatest healthcare needs will never materialize. Nor will the jobs to produce them. Commissioner Hamburg has called the FDA "America's Innovation Agency" (*Wall Street Journal*, August 1, 2011), which might be considered more an aspiration than historical fact. But it is an aspiration we share, and believe that PDUFA V will be an important step in accomplishing it.

Thank you again for the opportunity to testify. And I would now be pleased to answer any questions you may have.