

Dr. Josh Makower Testimony

My name is Dr. Josh Makower and I have dedicated the past 22 years of my life to developing therapies and technologies to improve patient care. Over this time I've founded 6 independent medical device companies which have created several hundred jobs in the United States and the technologies I have invented and developed have touched the lives of hundreds of thousands of patients across the world. I am an inventor on over 100 issued patents and on over 330 patent applications. Through the medical device incubator, ExploraMed, that I started back in 1995, our medical device companies have developed technologies to address conditions such as coronary and vascular occlusion, heart failure, incontinence, osteoarthritis, chronic sinusitis, chronic and acute otitis media, obesity, prostatic disease, and several other major medical conditions. ExploraMed receives support from NEA, a venture fund, where I also serve as a Venture Partner on the Medical Device team. NEA has been helping to build great companies since 1978. In addition to being a physician-inventor and entrepreneur, I am a Consulting Professor of Medicine at Stanford University and have co-founded the Stanford Biodesign Innovation Program to teach the process medical technology innovation to the next generation of innovators. This effort has graduated hundreds of students through our fellowship and course programs and now includes Biodesign Innovation collaborations with leading universities across the globe.

My reason for being here today is that I care deeply about patients and patient care and understand how acutely important medical technology innovation is to the advancement of the health and well being of our society. I am also here today because I am deeply concerned that we are in jeopardy of losing the US leadership position in medical technology innovation as a result of the current regulatory environment at FDA. Over the past few years it has been increasingly more difficult, more time consuming, more costly and *less* predictable to navigate the FDA approval process. As a result, investment is drying up, companies are moving overseas or closing their doors and US patients are being denied timely access to safe and effective new medical products. If this situation does not improve immediately, a generation of innovation and businesses will be lost, along with the jobs they would have created and the lives they would have saved or improved.

These concerns are not mine alone. Numerous studies and reports over the past year document the difficulty innovators are having navigating the FDA. In response to questions from Members of Congress and FDA officials regarding the scope of the problems, I, along with Abeed Meer of Stanford, conducted a survey of over 200 medical technology companies to generate data on their specific experience. So much of what has become policy over the past few years has been based on anecdotes and single examples and I felt compelled to bring data to this discussion. It is essential we use data to drive our decision-making. Recognizing that all studies have limitations, mine is no different; however, the results of my study are compelling and cannot be justifiably ignored or dismissed.

Before discussing the specific findings, it is important to have a better understanding of the medtech industry which plays an important role in the lives of patients around the world. In this context, medtech refers to medical devices intended for use for therapeutic and diagnostic

purposes. Together with other segments of the larger health care sector, medtech companies have contributed to dramatic improvements in health. For example, from 1980 to 2000, new diagnostic and treatment paradigms helped drive a 4 percent increase in life expectancy in the U.S., a 16 percent decrease in annual mortality rates, and a 25 percent decline in disability rates for the elderly.¹

The U.S. medtech industry also has an essential role in the U.S. economy. In 2006, companies in the field shipped products valued at \$123 billion and paid \$21.5 billion in salaries.² The industry directly employs more than 400,000 employees, and is responsible for over 2 million total jobs, including those that support this vibrant industry. Employees in the medtech field earn above average wages—approximately \$60,000 per year—because the industry requires and attracts a highly skilled and educated workforce.³ New medical technologies also have the potential to drive down costs in a world of escalating healthcare expenditures.

Internationally, the U.S. is the largest global consumer of medical devices. However, it is also the world's leading producer. The country achieved this leadership position through decades of strong, sustained investments in research and development (R&D) by U.S. medical device companies and the venture capital community that backs them. As a result, the medtech field is among a limited number of industries in which the U.S. maintains a trade surplus. In 2007, the total medtech trade surplus was estimated at \$5.4 billion.⁴

Traditionally, innovation in the medtech industry has been driven by small, entrepreneurial companies with a passion for discovering safer, more effective ways to diagnose and treat patients. Although a number of major device manufacturers exist, more than 80 percent of medtech companies have fewer than 50 employees.⁵ These small starts-ups are the engine that fuels the development of innovative new devices, which are often acquired by the larger companies. Through the combined efforts of both small and large medtech companies alike, R&D investment in the industry more than doubled during the 1990s, and it continues to outpace the R&D investment of companies in other U.S. manufacturing industries by an average of twice as much.⁶

However, over the past few years, navigating the FDA has become less predictable, more time consuming and more costly. As a result, we are losing our global leadership position in medical technology innovation.

¹ "The Value of Investment in Healthcare," MEDTAP International, 2004, www.aha.org/aha/content/2004/PowerPoint/ValuePresentation.ppt (October 2, 2010).

² "State Economic Impact of the Medical Technology Industry," The Lewin Group, 2010, http://www.ihif.org/files/State%20Impacts%20of%20the%20Medical%20Technology%20Industry_%23436092%200_3_.pdf (October 26, 2010), p. 1.

³ Ibid., p. 4.

⁴ "Medical Technology and Venture Capital: A Fruitful Yet Fragile Ecosystem," MDMA and NVCA, June 2009, <http://www.medicaldevices.org/node/656> (October 2, 2010).

⁵ Ibid.

⁶ "Medical Devices Industry Assessment," International Trade Administration, 2009, <http://www.ita.doc.gov/td/health/Medical%20Device%20Industry%20Assessment%20FINAL%20II%20203-24-10.pdf> (October 2, 2010).

In fact, just last month, PwC issued an innovation scorecard on medical technology innovation, and the message was dire. PwC looked at several factors in innovative nations, including the availability of investment resources and efficiency of regulatory systems. The study showed that it is clear that American innovators are going outside the U.S. first to seek clinical data and revenue. While much of this innovation is finding its way to European patients, the study notes that by 2020, it is likely that other nations such as Brazil, India and China will benefit from America's regulatory challenges. Simply put, we have no time to lose.

The FDA

Within the FDA, CDRH has two primary regulatory pathways that medical devices can take to get to market. The Center uses the premarket approval (PMA) pathway to evaluate and approve technologies that are truly novel and pose a high potential risk to the patients using them. For low to medium risk devices, it employs the premarket notification or "510(k)" process. Regardless of whether a device must follow the 510(k) or PMA pathway, the FDA has the ability to request that a company provide clinical data to support clearance or approval. This data often requires an allowance by the FDA to perform clinical trials in the U.S., which is known as an investigational device exemption (IDE).

Early in the implementation of section 510(k) of the Medical Device Amendments, it was well recognized that the 510(k) pathway to market could efficiently facilitate the availability of new technologies that have the same intended use as legally marketed devices without creating an undue regulatory burden. This approach was intended to allow companies to build upon established clinical and scientific evidence of safety and effectiveness to more rapidly iterate and improve the innovations available to patients. Not surprisingly, the 510(k) process is more widely used than the PMA pathway. In 2009, for example, CDRH approved just 15 original PMA submissions while it cleared approximately 3,000 products under a 510(k).⁷

As it shepherds technologies through these two pathways, the FDA must balance the imperative of assuring the safety, effectiveness, and quality of commercially available medical devices with its mission of fostering innovation by providing companies with a timely, predictable route to market. In recent years, some politicians, members of the press, and consumer groups have criticized the FDA for not adequately addressing the safety of medical devices, particularly those cleared through the 510(k) pathway. These concerns have persisted despite a lack of evidence that both the 510(k) and PMA pathways are not fulfilling their intended purpose of protecting patients. In fact, despite the anecdotal examples reported in the media, there is compelling evidence to the contrary. For example, one recent study demonstrated that approximately 99.6 percent of all 510(k) and PMA devices that were cleared/approved by the FDA from 2004 to 2009 have not been associated with a Class I⁸ recall.⁹ (Recalls are an indicator of major device problems that have the potential to negatively affect patient safety and/or device effectiveness.) Such results demonstrate that serious device-related safety problems are extremely rare. Also,

⁷ Calculated from FDA data available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm> and <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm> (October 22, 2010).

⁸ A Class I recall is the most serious type of FDA recall because the problem for which the device has been recalled may result in major injuries or death.

⁹ Hall, op. cit.

the data shows that the majority of these rare postmarket events stem from issues relating to quality systems and manufacturing processes and not issues that would have been most effectively detected through more expansive premarket clinical trials.

Despite this evidence, the FDA's clinical data requirements continue to rise. While the agency historically used the postmarket period to continue accruing data regarding device safety and effectiveness (allowing the market to determine the value of a medical device), it is increasingly demanding that this kind of large-scale clinical data during the premarket period. When it comes to premarket data requests for new products, medtech innovators say they face more uncertainty regarding the FDA's expectations, and that bench, animal, and clinical testing requirements are mounting without clear justification or benefit. Even more troubling are an increasing number of examples from industry representatives that FDA reviewers have requested esoteric scientific testing, or posed questions that are not reasonably answerable, sometimes at great expense and with little relevance to safety and effectiveness. Moreover, medtech innovators have reported that the FDA is becoming less predictable and increasingly inefficient in its premarket review role. Stakeholders maintain that the CDRH, over the last several years, has become even less transparent in how it makes decisions, as well as slower in responding to inquiries and regulatory submissions. The degree to which these reports represent isolated incidents versus a general trend was unknown prior to the initiation of the study I conducted.

According to device companies, changes at FDA have created nearly insurmountable barriers to medtech innovation in the U.S., with no apparent off-setting public health benefit. The current regulatory environment is particularly challenging for start-up companies – which have historically played a key role in driving innovation – because of their limited financial resources. As a result, regulatory submissions and clearances/approvals for innovative new medical devices are declining in the U.S. In an era of greater scientific knowledge and technology advancements than any other time in history, one must question what forces are driving medical technology innovation in a downward direction.

The purpose of the study was to gather quantitative and qualitative data from a representative subset of medtech companies to elucidate the impact of the FDA's current regulatory practices on medical technology innovation and the advancement of public health so that Congress, the FDA, and the IOM would have more information to consider it in their evaluation.

I have submitted the full study as a part of my testimony, but I want to highlight several powerful findings.

The study found that for low- and moderate-risk devices, the process to navigate the FDA took companies up to two years longer than it did for a similar approval from European regulators. For higher-risk devices, the discrepancy was greater -- in the U.S. , it took three and a half years, or five times as long as Europe, to grant approval.

By overwhelming majorities, companies reported that European regulatory authorities were more predictable and transparent than FDA. Almost half the companies reported that key FDA personnel responsible for reviewing their product changed during the course of the review, and

one-third reported that appropriate staff were not present at meetings between the companies and FDA to discuss review issues.

Given that it takes longer and costs more money to launch a product in the US, a reasonable question is what is gained from the additional time and costs that result from the FDA process.

A recent study conducted by the Boston Consulting Group answered this question. The report examined the rate of safety recalls for medical devices in Europe from 2005-2009 and compared them with the level of similar recalls in the U.S. It found that there is little to no difference between average recall rates in the United States and the European Union. Essentially, American patients and workers are getting none of the upside to today's regulatory environment, but all of the downside.¹⁰

It should be noted that neither I, nor my colleagues, oppose FDA asking for clinical data when the circumstances warrant. In fact, FDA currently has the authority to ask for data whenever they deem it necessary. The problem for medical technology innovators arise when the requirements change at FDA without transparency or without justification. This uncertainty is harmful to innovation, job creation and patient care because it stymies future investment in medical technology innovation.

Another critical issue is the severe decrease in investment funding for innovative medtech companies. Series A financings are a leading indicator for innovation and job creation in the medical technology industry. Unfortunately, due to today's current regulatory environment, the number of start-ups receiving this crucial funding is down almost 50 percent from two years ago. According to a PwC/National Venture Capital Association report, in 2008, 118 start-ups received Series A funding, while in 2010, this number dropped to 60. In order for innovative companies to drive job-creation and patient care, this trend cannot continue.

Implications to the U.S. Economy

Until recently, device innovation has largely been a U.S. phenomenon—the most important new technologies were invented here, and commercializing them in the sizable U.S. market was at the core most medtech company strategies. However, as medtech hurdles have climbed and available funding has declined, device companies are considering alternative strategies that are less U.S.-dependent. Unfortunately, as described, this means that many new technologies are reaching U.S. patients later than patients in other geographies. It also suggests that the United States is at risk of losing its premier position at the center of the global medtech innovation ecosystem. As this epicenter shifts, the U.S. economy will be negatively impacted as jobs are moved overseas.

Despite the fact that U.S. elected officials are calling for increased innovation and the high-quality, high-salary jobs associated with innovative industries, survey respondents verified in their comments that medtech jobs are moving offshore. For instance, one participant reported that his device company had recently set up overseas operations, firing 19 employees in the U.S.

¹⁰ <http://www.advamed.org/NR/rdonlyres/061A4AC8-D6A3-4960-826B-672214A0A623/0/REPORTBCGEuropeanUSSafetyFINAL.pdf>

and hiring 12 in Europe. Next, the company planned to shut down its U.S. production facility and move another 30 to 40 manufacturing jobs to Europe. In this particular example, all future growth was also planned overseas. Keeping in mind that every direct medtech job is indirectly responsible for another 4.47 jobs in the national economy,¹¹ the effect on U.S. employment could be sizable.

While the needs of an industry or the economy at large should never be prioritized over patient safety, it is not clear that the current regulatory obstacles to U.S. market entry that are imposed on medical innovators truly contribute to the protection and promotion of public health. Given the dire economic condition of the U.S. at the present time, the trend toward creating exceptional barriers for one of the few remaining industries in which our country is still a leader should be a significant cause for concern.

Looking Forward

Our nation currently faces unprecedented challenges in almost every sector of the economy. However, to individual citizens, nothing is more important than their own health and welfare, as well as the health and welfare of their families. Regulators and innovators have an important responsibility to protect and advance public health, and to maintain the balance between risks and benefits for the patients they serve. In doing so, the patient must remain first and foremost in our minds at all times. Patients can be harmed if unsafe medical technologies reach the market, but they are also harmed when important innovations are not available to treat their medical conditions.

The data presented in this report present a troubling picture of the state of medical device regulation (and its effect on innovation and the advancement of public health) under current FDA policies and practices. The survey results also indicate that the pendulum may have swung too far in one direction and balance again needs to be restored.

As noted, the changes at the FDA that have transpired over the last several years (and that have accelerated in the last two years) have largely been driven by perceived safety concerns. Yet, other than isolated examples and anecdotes, no collective data has been presented to suggest the need for such significant and sweeping adjustments. During this period, regulatory processes in Europe have remained relatively constant, making them a valuable comparator for our own regulatory performance in the U.S. It is clear from the data that the European regulatory process is more predictable, reasonable, and transparent. This system also allows companies to make safe and effective new medical products available to patients more quickly, and at a lower cost. If the same devices become available in U.S. following their European approval only after extensive delays and additional costs are accrued, we must evaluate whether the U.S. premarket regulatory process is truly contributing to the advancement and promotion of the public health, or if it is actually restraining it.

Today, as we face substantial concerns regarding the cost of healthcare, we also must acknowledge that a substantial number of important patient needs still remain unaddressed. A solution to both of these problems cannot be achieved by delaying new innovations and cost-

¹¹ See “State Impacts of the Medical Technology Industry,” op. cit., p. 12.

effective treatments. To truly promote the public health, the FDA must impose reasonable regulatory requirements on new innovations, implement more balanced requirements for premarket and postmarket clinical data, and go back to leveraging market forces to reward technology that presents the greatest value to patients. Only then will the most cost effective advances in medical care be delivered; and only then will the public health and our economy be best served.