U.S. House of Representatives, Subcommittee on Health Care, District of Columbia, Census and the National Archives of the Committee on Oversight and Government Reform

June 2, 2011

"Pathway to FDA Medical Device Approval: Is there a Better Way?"

Testimony of:

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Chairman Issa, Chairman Gowdy, Ranking Member Davis, and members of the Committee, my name is Jack Lasersohn and I am a general partner at The Vertical Group, a venture capital firm with offices in Summit, New Jersey and Palo Alto, California. My firm invests in innovative startup companies in the fields of medical technology and biotechnology. For more than 30 years, the principals of my firm have been founders, early stage investors, major shareholders and executives of many of the medical technology industry's most successful companies. These include the startups that developed ultrasound and MRI imaging, coronary angioplasty, minimally invasive spine surgery, artificial spinal discs, AAA stent grafts and beating heart CABG surgery. As a general partner of the firm, I serve on the boards of many companies with products either engaged in or preparing for FDA review.

In addition to representing my firm and its portfolio companies here today, I am also testifying on behalf of the National Venture Capital Association (NVCA) based in Arlington, Virginia. The NVCA represents the interests of more than 400 venture capital firms in the United States. These firms comprise more than 90 percent of the venture industry's capital under management. I currently serve on the Executive Committee of the NVCA Board of Directors and was a founding member of the Medical Innovation and Competitiveness Coalition (MedIC), which is a new organization under NVCA that brings venture capitalists, early-stage companies and entrepreneurs together to advance policies that will promote medical innovation and job creation in the U.S.

It is my privilege to be here today to share with you, on behalf of the venture industry and entrepreneurs, our perspective on the impact that FDA performance has on innovation in the U.S. medical devices industry. During most of my 30 years as a healthcare venture investor, our government has partnered with entrepreneurs and investors to safely speed innovative new devices to market, where U.S. patients can benefit from their use. Over this time, the U.S. grew into the undisputed center of global medical innovation and Americans were first in line for the life-saving and life-changing devices that U.S. companies produced.

For decades, venture capital has provided the fuel for U.S. medical innovation. Virtually every major new medical device and biotechnology drug from the last 30 years was developed by a U.S. start-up company and funded by venture capital. Venture-backed innovation has an impressive track record of spawning entirely new industries, as it did with biotechnology and personalized medicine, and thus provides a major source of job creation. In addition, small, venture-backed companies have served as the de facto research and development pipeline for larger medical device manufacturers, who buy startups, their products and the research that went into developing them only after venture backing has shepherded these companies through their riskiest stages.

Unfortunately, the environment that allowed these innovations to flourish has changed significantly over the last decade. Today, America's medical innovation ecosystem has come under intense strain. Although revolutionary research is ongoing, fewer groundbreaking medical devices are making it to the marketplace, and those that do make it are taking longer and costing significantly more to get there. As a result, investment in medical devices is beginning to dwindle. In fact, since 2008, total annual venture investment in the medical devices sector has declined by $1 billion. The economic downturn has certainly impacted investment in the life sciences space; however, changes in the U.S. regulatory environment over the last several years have also played a role.

In addition, there is a small but vocal minority in the community, the press and in Congress who are beginning to question the value of medical technology innovation in general. For example, coronary stenting is criticized for not providing a mortality benefit in "stable" cardiac

patients when compared to aggressive drug therapy. However, this narrow perception completely ignores the substantial benefit of stenting in reducing angina and improving quality of life for such patients.

Moreover, the 'aggressive drug therapy', that now clearly does improve mortality in stable patients, is itself the result of decades of astonishing innovation in pharmaceuticals, such as statins and ACE inhibitors, another vital part of America's medical innovation ecosystem.

Similarly, in the large portion of the population with 'unstable' cardiac disease and heart attacks, primary treatment by DES stenting, and vastly improved CABG surgery, provide clear and dramatic mortality benefits. In fact, the enormous improvement in mortality and morbidity due to coronary disease over the past thirty years, which every American is well aware of, has been due in great part to technological innovation, as well as the public health initiative to reduce smoking. This attack on innovation predicated on a narrow view of benefit is highly misguided and fosters an atmosphere that is increasingly hostile to entrepreneurial risk taking and may contribute to increased FDA risk aversion.

These environmental changes are beginning to stifle the economic growth and job creation that this industry has fueled in the U.S. for so many years and made our nation a world leader in medical device innovation, to the enormous benefit of the American public and patients.

At the same time, other countries have emulated our model – from financing methods to clinical research infrastructure – and have begun to draw innovators and capital away from the U.S. As a result, we are starting to see stagnation within the U.S. innovation ecosystem. Increasingly, seriously ill patients must wait in line behind patients in other countries for the groundbreaking devices they so urgently need – even when those devices were originally developed by U.S. companies. Percuataneous heart valves are the latest example of this unwelcome trend. Worse, a growing body of research suggests that the performance of the FDA has played a direct role in this decline. For most entrepreneurs and investors, the process has grown unpredictable – if not inscrutable. Working on short resources to fulfill a broad set of responsibilities, FDA personnel struggle to keep up with their workload. The effect can be frustrating and demoralizing for all parties.

Research provides the context for change

Many of my colleagues in the medical innovation ecosystem and the larger innovation economy have shared recent data and insights with Congress that provide evidence of this concerning trend. I believe it will be beneficial, for purposes of context, to briefly review the findings of some recent and important research on our topic today and I have summarized them below. I believe this research not only identified challenges, but also points to solutions.

"FDA Impact on U.S. Medical Technology Innovation, A survey of over 200 medical technology companies." (November 2010) In surveying more than 200 medical device startups on their experiences with FDA reviews, Stanford University's Dr. Josh Makower found that it took companies up to two years longer to navigate the FDA approval process for low- and moderate-risk devices, as compared with the same process in Europe. For high-risk devices, the FDA process took five times longer than the corresponding approval process in Europe. A significant majority of companies also characterized the European regulatory process as more predictable and transparent than the FDA's. Finally, nearly half of respondents indicated that key personnel assigned to their review by FDA changed during the review process, while one-third indicated that appropriate FDA staff did not attend meetings set up between the company and FDA to discuss review issues.
http://www.medicaldevices.org/node/846

"EU Medical Device Approval Safety Assessment: A comparative analysis of medical device recalls 2005-2009." (January 2011) Conducted by the Boston Consulting Group, this study compared public data regarding severe recalls of medical devices in Europe vs. in the U.S. over a four year period. It found that the number of such recalls was identical to that in the U.S. The conclusion was that the standards in place in Europe have not led to greater numbers of safety issues or recall rates versus the U.S., and that increasingly U.S. consumers have been sacrificing timely access to the most innovative devices without a corresponding gain in overall health or safety.
http://www.advamed.org/NR/rdonlyres/061A4AC8-D6A3-4960-826B672214A0A623/0/REPORTBCGEuropeanUSSafetyFINAL.pdf)

"Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry." (February 2011) This study, conducted by the California Healthcare Institute and Boston Consulting Group, examines the impact of FDA performance on U.S. competitiveness in the global medical innovation ecosystem since 2007. It found that review and clearance times for medical devices have increased significantly during this time – driven in part by the addition of new responsibilities assigned to the agency by Congress. Concurrently, a number of "high-profile safety problems" prompted the agency to give disproportionate weight in its risk-benefit analyses to mitigating potential risks rather than to the benefits of getting new technologies to market in a timely fashion. The result has been a U.S. regulatory process that discourages medical innovation and investment. Meanwhile, competing countries have streamlined their regulatory processes to draw U.S. companies abroad.
http://www.chi.org/uploadedFiles/2011%20CA%20Biomed%20Industry%20Report_FINAL.pdf

"Medical Technology Innovation Scorecard: The race for leadership." (January 2011) Conducted by PricewaterhouseCoopers (PwC), this study revealed three trends that bode poorly for future U.S. global leadership in medical device innovation. First, innovation is beginning to migrate overseas as more technologists and entrepreneurs build their companies, conduct their clinical trials, register their products and enter the marketplace in countries other than the U.S. Second, patients in foreign markets are beginning to benefit from advances in medical technology before their American counterparts with increasing frequency. Third, emerging-market countries are practicing a fundamentally different form of innovation that emphasizes "smaller, faster and more affordable devices" that reduce healthcare costs system-wide.
http://www.pwc.com/us/en/health-industries/health-research-institute/innovation-scorecard/index.jhtml

The overarching message delivered by all of these reports is unmistakable: The U.S. is losing its competitive lead in medical innovation, and will continue to do so unless lawmakers, regulators, and the private sector work together to bring the FDA's risk-benefit analysis back into balance.

Today, I would like to use this opportunity to provide recommendations on how innovators, investors and policymakers can work together to recalibrate the FDA's approach and regain

America's competitive edge in the field of medical devices, and more importantly, ensure that providers and patients have timely access to innovative therapies. Although my comments are focused on medical devices, it is important to clarify that NVCA and MedIC believe that any FDA reform efforts should focus on both the medical device and the drug/therapeutics regulatory process. NVCA would be happy to provide our recommendations for improving the regulatory process for drug/therapeutics at the appropriate opportunity.

NVCA's Recommendations for Change

Overview

Historically, the FDA has played two parallel roles in the U.S. medical innovation ecosystem. The first has been to assure the safety, quality and efficacy of medical devices for public use. This role is explicitly mandated by law. The second, which is not mandated in FDA law but has grown out of the agency's execution of the first role, has been to ensure that American patients have access to the most innovative treatments and technologies by providing a timely and predictable path to market. In balancing these roles, the agency has promoted the general health of the American people for decades.

The venture capital community supports the FDA in both of these roles and views the agency as a partner in bringing innovative treatments and devices to the American public. My colleagues and I are encouraged by the FDA's willingness to address many of the challenges revealed or confirmed, as the case may be, by the research I describe above. The challenges identified in the research present opportunities for action, and we want to be partners in developing positive changes to the FDA review process – changes that will put innovative medical devices in the hands of doctors and patients more quickly and safely than it does today.

The FDA took a first step in this regard in January, when it announced its Medical Device Innovation Initiative (MDII). NVCA applauds the FDA for recognizing the importance of establishing a collaborative, efficient and predictable regulatory review process for novel, life-saving technologies. Now, implementing this initiative in a rational and effective manner so that it can meet its stated objectives will be critical. We believe that maintaining America's competitive edge in medical innovation depends on it.

Venture capitalists also understand the enormous difficulty of the FDA's task. Medical devices are more complex than ever before, and the rate at which this complexity grows continues to accelerate. We also believe that the FDA needs more resources in order keep up with the speed of innovation. Attracting and keeping the talent required to do so is difficult under the agency's current budget constraints – a reality that the Makower study illustrates. We understand that resources are a challenge, given the overall U.S. budgetary situation, and we acknowledge that every expenditure will be and should be scrutinized for its effectiveness. However, we cannot let these difficulties serve as excuses for inaction or acceptance of decline.

Rebalancing FDA's Risk-Benefit Analysis for Medical Devices

As I mentioned earlier, the research suggests that FDA's risk-benefit analysis for novel medical devices has grown out of balance relative to its past practices and relative to current practices in other countries – especially in Europe. There are two major steps that the FDA can take to bring its risk-benefit analysis back into balance. Each pertains to the type of device under review.

510(k) devices

For devices the FDA deems as posing a low to moderate potential risk to patients, the agency employs a premarket notification process, also called the 510(k) process. Such reviews often involve new or improved devices that have the same intended use as existing devices, and they allow companies to build on established scientific evidence of safety and effectiveness.

In the cases of Class I and Class II 510(k) devices, the FDA should significantly expand its use of certified third-party entities for reviews. As the research suggests, this practice is used widely in Europe without incurring a premium in lost safety performance. The members of these reviewing entities are certified and noted experts.

In the U.S., third-party boards could handle as much as 50 percent to 75 percent of 510(k) reviews. Such a shift would significantly reduce the resource burden on the FDA because the agency could redirect its efforts to reviews of pre-market approvals (PMAs) and higher-risk 510(k) devices. In all cases, the FDA would have the right to pull back any cases considered by an approved third-party for further review as it deems necessary.

Pre-Market Approvals (PMAs) and higher-risk 510(k) s

For truly novel devices or for devices that may pose a high potential risk to patients, the FDA employs a pre-market approval, or PMA, pathway. This review process is more extensive and usually requires that companies conduct clinical trials to demonstrate efficacy and safety.

Under current law and in medicine in general, safety is not defined as the absence of risk, but rather as a reasonable assurance that the probable benefit of using a device exceeds its probable risk. Effectiveness is defined to require that the benefit be clinically significant, which means it must produce a clinically meaningful improvement in the health of a significant proportion of the population in which it is used.

For PMAs and Class III 510(k) devices, the FDA should establish, as a general principle, that reviewers employ a much more flexible risk-benefit analysis than what is currently in use. This means that while the general requirement that benefit exceed risk will always apply, the specific threshold for each of the elements within that analysis will change depending on the clinical context for the specific device. The review should take into account the incidence and severity of the disease at issue, whether there is an urgent and unmet need in the marketplace, and any potential safety issues. The FDA should make clear to its reviewers that this calculus is explicitly adjustable.

These adjustments might include, for example: reducing the level of evidence required to provide "reasonable assurance" and assessing what is a "clinically meaningful" improvement in health or what proportion of a population is deemed "significant" in a more targeted manner.

In addition, the FDA should measure probable benefits against probable risks, as the law currently requires. This contrasts with the practice of requiring some "absolute" high level of benefit to insure against a "possible", hypothetical, risk to health in the broader population, which appears to be the FDA's emerging practice. This latter approach is a theoretical exercise that will lead to regulatory paralysis.

We should combine this flexible, common-sense approach with an expanded FDA mission to explicitly include the promotion of medical innovation. Medical breakthroughs follow a well-established learning curve. They usually begin with only a small advantage over the status quo, and then dramatically improve over time. This was certainly true for coronary angioplasty and all forms of medical imaging. In fact, it has been true for virtually all major medical innovations over the past 50 years. Requiring that all novel products meet some "absolute" threshold of risk/benefit, particularly when they are first introduced, can derail many promising new ideas.

The FDA will argue that it already employs a flexible risk-benefit approach. We agree that it does in some cases and, when it does, the system works very well. However, the research data I cited suggests that this is not its common practice, or that it is not being applied uniformly in all cases. We believe that endorsing this flexible approach in legislation, combined with a strong legislative directive to promote innovation, will enable the senior management of FDA to standardize this approach throughout the Agency.

This type of flexible risk-benefit analysis is not without precedent here in the U.S. In fact, it has generated some extraordinary results in the pharmaceutical space. For example, in the cases of HIV and cancer therapies, Congress explicitly recognized the need to adjust the risk-benefit analysis as health crises began to unfold around these two diseases. As a result, the accelerated approval process for drugs in those diseases has been extremely successful and should be expanded, as I discuss below.

Other Opportunities for Reform at FDA

In addition to the recommendations above, NVCA MedIC is advocating for a number of broader reforms at FDA. While these are not exclusive to medical devices, I believe they are relevant to our discussion today. They are:

Strengthen FDA Mission and Structure. As I mentioned before, Congress should amend the FDA's statutory mission to explicitly include promoting public health through acceleration of access to novel therapies and technologies. Congress should also require the agency to routinely assess the impact of its decisions, policies, and priorities on unmet medical needs and medical innovation using agreed upon metrics. This process should be collaborative and

transparent with the public. The agency's mission should be clarified to strengthen the role of healthcare providers in decision-making so that doctors, rather than the FDA, act as the arbiter of what products are cost-effective in the marketplace.

Ensure that Individuals with Significant Expertise can Participate as Advisory Committee Members. In its current Advisory Committee structure, the FDA is often unable to access the best expertise to evaluate breakthrough therapies and technologies because of the tightening of its conflict of interest rules. Let me assure you that NVCA understands and appreciates the important need for rules to guard against conflict. However, we are deeply concerned that the current rules have made it nearly impossible to recruit qualified scientific experts who have the knowledge and understanding of clinical trial design, analysis, and drug and medical device development expertise. Without this expertise, FDA Advisory Committee members face significant challenges in making decisions on innovative products. This situation is stifling the advancement of novel therapies and technologies, leading to delays in access for patients.

The statutory cap on conflict of interest restrictions should be amended to permit qualified experts to serve on Advisory Panels (but, perhaps, with more limited voting authority). Experts should be transparent and provide full disclosure of conflicts. The FDA should have the ability to recruit more widely from non-academic pools of candidates who have the expertise to evaluate medical products. Similar to the requirement of a patient representative, all Advisory Committees should include an "Innovation Advocate" drawn from the community of investors and/or entrepreneurs who finance medical innovation.

Streamline the Regulation of Cross-Cutting Innovation Including Regulatory Pathway for Personalized Medicine. The FDA's current classification for drugs, biologics and medical devices (which include diagnostics) is ill-equipped to keep pace with the direction of cross-cutting medical innovation. This is particularly evident in the area of personalized medicine, which is bringing cross-cutting therapies together in radically new ways to help develop more effective treatments for individual patients. There is currently no structure to evaluate these personalized medicine approaches, which often combine diagnostics with

therapies, or therapies with devices, despite the fact that this area of lifesciences represents some of the most promising medical innovations of the next century.

The FDA should promote the development of personalized medicine through a well-defined regulatory pathway for approval of new therapeutics and companion diagnostics or drug-device combinations. For example, in the area of cancer therapy, the FDA should be required to provide guidance on the targeted approval process, and a manual of policies and procedures for administrative coordination of interactions between the sponsor, the Center for Devices and Radiological Health (CDRH) and the Center for Drug Evaluation and Research (CDER).

Conclusion

I'd like to conclude my testimony by reiterating that the U.S. has led the world in developing and marketing innovative medical devices for decades. If we act now to implement policies and regulatory reforms that bring the risks and benefits of novel technologies back into balance, we can revive the U.S. medical innovation ecosystem and ensure that seriously ill patients continue to have access to breakthrough therapies and technologies in a timely fashion.

I want to personally thank you for the opportunity to discuss these important issues with you today, and to thank you for your service to our country in your capacity as Members of Congress.