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**Testimony of Michael A. Mussallem
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“21st Century Cures: Examining Barriers to
Ongoing Evidence Development and Communication”
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Introduction

Chairman Pitts, Ranking Member Pallone and Members of the Subcommittee:

I am Mike Mussallem, chairman and CEO of Edwards Lifesciences, based in Irvine, California.

I am truly honored to join my fellow panelists today to discuss a path to revitalizing medical device innovation in the United States.

I am here because I am passionate about helping patients. That’s why I and hundreds of thousands of U.S. medical device company employees like me come to work each day. We love what we do because it can have such an amazing impact on Americans’ quality of life.

Based on Edwards’ experience in developing and delivering new therapies to American patients over the last several decades, I am very concerned that we are seeing an alarming and documented decline in U.S. medical innovation¹, as this Subcommittee has heard previously. The balanced ecosystem that has supported innovation in the U.S. is being eroded by an increasingly costly and cumbersome risk-averse culture in our regulatory and payment systems.

Our recent experience with the development of an innovative heart valve replacement therapy, which enables a team of physicians to replace a patient’s aortic heart valve without open-heart surgery, has provided us a unique perspective on the current regulatory process. During the last decade, as we have navigated the regulatory channels to bring this therapy to U.S. patients, we have

¹ National Venture Capital Association. (2014). *NVCA 2014 Yearbook*. Arlington, Virginia: Thomson Reuters.

taken note of not only the challenges, but also the forward-looking vision of the leaders of FDA and CMS to develop opportunities for better collaboration with the agencies. We believe there are several opportunities to remove barriers in regulatory approval and reimbursement that will help promote America's continued worldwide leadership in the area of medical device development. While we have a number of recommendations for improvements that could be made, today I will focus on three primary areas:

- Evidence development mechanisms can be improved to reduce costs and delays.
- Economic incentives need to be aligned with promoting innovation.
- FDA's vision to improve the regulatory process must be accelerated.

Our Unique Perspective

Over the 35 years I have spent working in medical devices, I have had the opportunity to be involved with the development of dozens of innovative therapies for the treatment of heart valve disease and the critically ill. I am privileged to lead the more than 8,700 employees of Edwards Lifesciences, who dedicate their lives in a very personal way to helping patients around the world. We have been the leaders in heart valve innovation for more than 50 years, starting when an engineer, Miles Lowell Edwards of Santa Ana, California, partnered with a cardiac surgeon, Dr. Albert Starr of Portland, Oregon, to develop the first commercially available artificial heart valve. I have also had the honor of representing our industry in a number of leadership roles, noteworthy among them my term as chairman of the Advanced Medical Technology Association (AdvaMed).

It is my experience that successful medical device innovators keep an unwavering focus on patients. We count it a privilege to serve these patients, creating and supplying devices and therapies that save, enhance and prolong lives. We are the toolmakers for clinicians, working closely with them to develop technologies to address unmet patient needs. Each new innovation is also a stepping stone that lays the path to something even better. Innovation is a powerful and iterative force, and

those who are involved in it are never satisfied with the status quo. It is our passion and mission to keep finding better solutions to improve human health.

Edwards' innovation story is similar to many companies that have made medical technology a uniquely American success story. In just the most recent decade, between 2000 and 2010, medical advancements helped add nearly two years to U.S. life expectancy². Specifically, fatalities from heart disease were cut by a third; deaths from stroke were reduced by more than a third; and mortality from breast cancer was cut by almost a fifth³. Medical technology has been a strong contributor to the U.S. economy, responsible for about 1.9 million U.S. jobs, including both direct and indirect employment, and nearly \$150 billion in direct economic output (sales)⁴. Clusters of innovation in states like California, Texas, Minnesota, Massachusetts, New York and North Carolina, are responsible for addressing the world's most serious health challenges, while at the same time serving as a robust economic engine, providing attractive U.S. jobs and economic growth far into the future.

The success of these companies, and the existence of these clusters, is not by happenstance. There are a few essential elements to fostering an ecosystem that incentivizes curiosity and rewards innovators who develop new therapies for patients:

- Patient/physician need
- Ready access to capital and supportive economic climate
- Functional/timely/predictable regulatory processes
- Reimbursement system that welcomes novel therapies as they undergo a continuous improvement process
- Strong intellectual property protection

² National Center for Health Statistics. "Health, United States, 2012: With Special Feature on Emergency Care." Hyattsville, MD. 2013.

³ Ibid.

⁴ "The Economic Impact of the U.S. Advanced Medical Technology Industry," Battelle Technology Partnership Practice, March 2012.

Advancements in medical technology can also yield savings across the health care system by replacing more expensive procedures, reducing hospital stays and allowing people to return to work more quickly. Between 1980 and 2010, advanced medical technology helped cut the number of days people spent in hospitals by more than half⁵.

Edwards Lifesciences has been at the forefront of an extraordinary opportunity to impact the lives of patients suffering from a deadly heart valve disease called aortic stenosis. The Edwards SAPIEN transcatheter aortic heart valves deliver a collapsible prosthetic valve into the body via a catheter-based delivery system. The valve is designed to replace a patient's diseased native aortic valve while the heart continues to beat – avoiding the need to saw open the patient's chest, connect them to a heart-lung machine, and stop the heart. Those of you who have a friend or relative who's had open-heart surgery know first-hand how difficult this procedure and its arduous recovery can be. Our new heart valve allows patients to avoid that pain and suffering.

Some patients who receive the SAPIEN transcatheter valves can leave the hospital and go to their own homes the next day. It's extremely gratifying to hear physicians and patients describe the immediate improvement in patients' health after TAVR. They can breathe and speak more easily, their skin transforms from gray to pink as their vital organs once again receive the oxygen-rich blood they need, and their vibrancy returns within hours. In reporting the results in 2010 of a quality-of-life sub-study with the SAPIEN valve, David J. Cohen, M.D., M.Sc., Director of Cardiovascular Research at St. Luke's Mid America Heart and Vascular Institute, said, "The degree and immediacy of the quality of life improvement was striking, with significant benefits seen as early as one month. By one year, patients experienced both cardiovascular and physical health benefits, with the physical improvements roughly

⁵ National Center for Health Statistics. (2013, March 14). Table 103 – Discharges, days of care, and average length of stay in nonfederal short-stay hospitals, by selected characteristics: United States, selected years 1980 through 2009-2010. Retrieved March 15, 2013, from Centers for Disease Control and Prevention: <http://www.cdc.gov/nchs/data/hus/2011/103.pdf>.

comparable to a 10-year reduction in age. Quality of life is critically important, particularly for patients like those in this trial – and they are not just surviving, but also thriving.”⁶

Patients receiving the Edwards SAPIEN valve go home with potential years of good health added on to their lifespan. Extensive study of this valve – including an unprecedented record of four *New England Journal of Medicine* papers – has demonstrated the “triple win”: a substantial and sustainable clinical benefit, extraordinary quality-of-life improvement, and cost effectiveness in inoperable patients. In fact, the SAPIEN valves are the most studied heart valve in history, with more than 300 peer-reviewed, published articles on clinical outcomes associated with the valves. There are also more than 120 cost-effectiveness and quality of life articles related to transcatheter aortic valve replacement (TAVR).

While our experience with the SAPIEN valves and TAVR has ultimately been successful, it is important to reflect on its unique and challenging regulatory pathway, including some key milestones:

- In 1999, Edwards began an internal program exploring transcatheter valve replacement.
- In 2002, Professor Alain Cribier performed the first-in-human procedure of a transcatheter aortic valve replacement in France.
- In 2007, the Edwards SAPIEN valve, our first commercial transcatheter heart valve, received CE Mark for European commercial sale. The next-generation SAPIEN XT valve received CE Mark in 2010.
- Before SAPIEN was approved by FDA, CMS took the unusual step of initiating a National Coverage Determination (NCD) in October 2011.
- Four years after obtaining CE Mark in Europe, the SAPIEN valve was approved by FDA in November 2011 for the treatment of inoperable patients, making the U.S. the 42nd country in the world to approve the device.

⁶ Edwards Lifesciences. (2010). Edwards SAPIEN Transcatheter Heart Valve Demonstrates Substantial Improvement in Quality of Life in Inoperable Patients [Press release]. Retrieved from <http://www.edwards.com/newsroom/Pages/NR20101115.aspx>

- We achieved an additional regulatory approval in 2014 that means today, U.S. patients benefit from our second-generation device, during approximately the same time that our even more advanced third-generation device was launched in Europe.

As we have continued to innovate new generations of transcatheter heart valves, the U.S. has trailed Europe and other regions of the world in approving these more advanced valves. We believe FDA leadership has viewed this as an opportunity to identify improvements and seek helpful changes to the regulatory system that can improve, and shorten, the approval timeline for future generations of transcatheter heart valve devices.

We've appreciated the productive relationship with Dr. Jeff Shuren and the team at CDRH/FDA, along with Dr. Patrick Conway and colleagues at CMS, whose approach ensured that there was a balanced and reasonable review process for this transformative therapy. At FDA, Dr. Shuren's team worked to develop a post-approval study that allowed us to use registry data to satisfy our postmarket surveillance requirements. While Edwards did not request a formal parallel review process, CMS' early engagement was unique and demonstrated that the agency could move in an expedited fashion. Ultimately, Dr. Louis Jacques on Dr. Conway's team worked to develop a "flexible" NCD, which provides coverage for current *and* future approved TAVR indications and devices – although iterative therapies are best left to clinician judgment using existing payment pathways.

Lessons Learned

Evidence Development Mechanisms Need Improvement

To support regulatory decisions for approval and reimbursement of new medical technologies in the U.S., manufacturers are required to gather a great deal of clinical and economic evidence. Evidence development can be an extremely costly endeavor at each stage of the process. Often the cost to the system and inevitable delays that result are not a critical consideration for regulators. We've invested more than 10 years in just the pursuit of U.S. approval for the SAPIEN platform, dedicating time, resources and significant funding to product development, clinical trials and data collection and analyses. Focus should be put on reducing the delay and expense that data collection adds at every step in the process.

FDA has recently proposed a number of improvements to the premarket clinical trial process that hold promise, many of which have already been discussed by this Committee during previous 21st Century Cures hearings. Some of these improvements that we support include:

- Streamlining the investigational device exemption (IDE) approval process to reduce IDE approval timeframes.
- Reducing the legal complexity and inconsistency between each hospital Institutional Review Board (IRB) through the creation of a centralized or standardized review process.
- Incorporating patients' voices and tolerance for risk into the regulatory decision making process – from clinical trial design to PMA approval review.
- Addressing potentially duplicative clinical evidence through the consideration of surrogate endpoints and greater use of data developed outside of the U.S.

We also see opportunity for innovation on the postmarket side. Under the TAVR NCD, CMS requires that every U.S. patient be enrolled in a qualified prospective registry that tracks appropriate outcomes data to the patient level. In a remarkable effort of collaboration between the medical societies, regulators and other interested stakeholders, the American College of Cardiology (ACC) and

the Society of Thoracic Surgeons (STS) helped build what has become one of the most robust clinical evidence and quality measurement tools ever created: the STS/ACC TVT Registry. In my view, when registries are done right, they can yield extremely useful information about patient outcomes and device benefits. Access to more data more quickly can help patients and clinicians more accurately weigh risks and benefits of a procedure, and also helps inform new physician training and device design. For example, data from the STS/ACC TVT Registry for transcatheter aortic valve replacement procedures were used to follow patients, report on outcomes and ultimately help expand the indications for use of our SAPIEN technology, allowing access to a broader patient population.

However, the clinical and scientific benefits of registries must be balanced with their potentially significant cost, complexity and potential for misinterpretation and misuse of the data. We've seen through the vaccine debate what can happen when misused data, or data in the wrong hands, can keep therapies from helping patients. Too often, well-intended advocates have driven sensational headlines, citing cherry-picked data or anecdotal incidents that have received outsized attention. In clinical trials, sample sizes and statistically based clinical endpoints are created to ensure data cannot be manipulated later. Investigators are blinded to the outcomes until the predefined milestones are met. These basic scientific principles are the cornerstone of clinical research and prevent conclusions that are not statistically supported.

The burden and cost of complying with registry requirements is not insignificant. For example, the patient data registry form for the STS/ACC TVT Registry for transcatheter aortic valve replacement procedures is eight pages long and consists of more than 300 separate fields, requiring special staffing, and dedicated personnel, and hours of work to complete this exhaustive form. Many physicians have told us that it takes longer to fill out the TVT Registry form than it does to perform the procedure. In addition to the significant financial commitment manufacturers must make to support the development and ongoing operations of registries, hospitals are charged ongoing fees to participate.

In a time of extreme budget pressure, we need to ensure that this process is not so costly and burdensome that the long-term prospects of the registry diminish over time.

Because of the potential for registries to increase the costs and burdens of healthcare delivery, we support AdvaMed's position that a number of "threshold questions" should be answered before determining whether a registry is the appropriate mechanism for meeting the defined objective:

- Are there already reliable data collection instruments available to collect the data needed to achieve the objectives?
- Will the registry have a stable and diverse source of funding to promote long-term sustainability?
- Is using a registry the least-burdensome means to collect the necessary data to achieve the scientific objectives?
- Do the objectives warrant the level of investment required to develop and maintain a registry?

In addition, the AdvaMed principles outline several key elements that should guide the development of any medical device registry, including: establishment of a data governance committee to oversee issues on ownership, as well as access to and use of any data collected; prospective registry design, to establish clear objectives and data analysis plans; policies for sharing of data collected with qualified scientific or medical researchers; and policies for the use and publication of registry data.

Economic Incentives Must be Aligned to Incentivize Innovation

Our legal and regulatory framework has created an increasingly challenging environment for innovation over the past several years. Unfortunately, efforts to curb healthcare spending could have the unintentional consequence of sweeping up innovation in a cost-cutting frenzy. For example, accountable care organizations (ACOs) and bundling payment models, while interesting for traditional procedures to treat established diseases, have the potential to incentivize providers to restrict access

to new therapies that may address an unmet patient need. If implemented successfully, such reforms could help ensure that patients receive better-coordinated and higher quality care, while also restraining rising costs. If implemented poorly, hospital value-based purchasing strategies could tilt toward simply restricting access and creating new barriers for patients and physicians as they seek advanced, clinically appropriate care.

It is imperative to recognize that medical device innovations become more effective and more efficient with time, experience and device improvement. If we hold new innovations to the same unforgiving standard that we hold well-established technologies that have been honed to near perfection over decades, we will miss opportunities to help American patients with new and transformational technologies. As toolmakers, we gather a lot of feedback on our first generation technologies, find opportunities for improvement, iterate and make it better. There is a learning curve, and we need a system that takes this into account and does not shut the door to evaluation on day one, while always maintaining patient safety along the way.

One effort that intends to provide earlier access to promising new therapies is Medicare's use of Coverage with Evidence Development (CED). When utilized properly, CED can be a useful tool for our reimbursement system. CED is a mechanism to provide coverage for new technologies that CMS doesn't believe reaches the "Reasonable and Necessary" threshold. However, CMS should be careful that CED does not become more of a burden to patient access than a tool for data development, particularly in cases where sufficient clinical evidence has already been developed – if so, the evidence requirement simply adds unnecessary time and cost.

I've had colleagues at other companies, as well as clinicians, ask me if our rigorous PARTNER Trial did not demonstrate "Reasonable and Necessary," how can we expect other technologies to meet this threshold? While CED has provided CMS with the ability to mandate hospitals submit data to the TVT Registry, any CED mandate should be removed once careful evaluation of the ongoing data supports continued coverage.

FDA's Vision to Improve the Regulatory Process Must be Accelerated

FDA is already taking on a number of initiatives to improve the regulatory processes to help improve patient access to innovative therapies. Thanks to the Food and Drug Administration Safety and Innovation Act (FDASIA), FDA has agreed to improved review and approval performance metrics tied to dramatic increases in manufacturers' user fees, and we are just beginning to see positive performance. Beyond that, during the last few years, Dr. Shuren and his team at FDA have outlined strategic priorities to strengthen the clinical trial enterprise, striking the right balance between premarket and postmarket data collection and improving customer service. Over the past year, a number of guidance documents have been drafted to provide manufacturers and FDA reviewers more clarity, including:

- Priority review for premarket submissions
- IDE and IRB approvals
- Patient preferences and benefit-risk analysis for premarket devices
- IDEs for Early Feasibility clinical studies
- Balancing premarket and postmarket data collection
- Expedited access for certain premarket approval devices

In addition, FDA's expanded efforts to improve device quality and safety by shifting the focus from the old regulatory compliance approach to an upfront quality assurance effort through its "Case for Quality Initiative" is promising. Finally, FDA's efforts to improve its regulatory management processes and structure through the recommendations coming from its Program Alignment Group is an important step in the right direction.

The biggest issue here is that FDA needs the resources and support to move faster on these initiatives. Drs. Hamburg and Shuren have a complex bureaucracy to manage, and they need the mandate to make change quickly. Congress could lend support to FDA by providing additional resources to FDA to help expedite these changes and give them room to innovate.

The TAVR Patient Experience

No discussion about medical technology is complete without understanding the true impact medical advancements have on patients – and we meet a lot of patients. I'd like to share one story of an Edwards SAPIEN transcatheter valve patient I have had the honor of coming to know during the last several years:

Lester Tenney is a true American hero, a part of our Greatest Generation.

As a tank officer in the Pacific Theater in World War II, Lester fought the Japanese in the Philippines before being taken as a prisoner of war in 1942 and forced to participate, along with 78,000 other soldiers, in the 85-mile trek that has since become known as the Bataan Death March.

Lester chronicled his experience in an inspiring memoir, *My Hitch in Hell*.

Having written this book about his unlikely survival, Lester's primary cause has long been the Japanese government's recognition of, and apology for, the suffering experienced by their prisoners of war.

In 2009, after decades of pursuit by Lester, the Japanese government agreed to sponsor a group of former prisoners of war to travel to Japan and receive that apology. The only problem: Lester's heart was giving out. Lester was having chest pain and couldn't catch his breath. The aortic valve in his heart had started to narrow and harden from aortic stenosis. Lester was 90 and had already undergone triple bypass surgery 20 years prior, so his doctors didn't think he could survive another open-heart operation.

Like all other aspects of his life, Lester was tenacious and sought another answer. He refused to accept that nothing could be done to address his aortic stenosis. Through his own research, he found out about TAVR and pursued this treatment option.

Lester had a transcatheter valve replacement in the spring of 2010 as part of a clinical trial at the Scripps Clinic in San Diego, and was discharged less than a week later. As a result of this life-saving procedure, Lester traveled to Japan with a group of six veterans, who met with parliament,

dined with Ambassador Roos, and, in an incredibly important victory, received a formal apology from Japan's foreign minister.

Today, Lester is at work on a new book, *The Courage to Remember*, which has a message of healing – in his case, this means healing from the PTSD of his war-time experiences and also his recovery from TAVR.

Lester and the tens of thousands of other patients we've had an opportunity to help remind us in the U.S. medical device industry daily that our work is personal, and it impacts people individually. Each heart valve represents a patient and their family, who otherwise would miss out on both the extraordinary and precious ordinary experiences of their daily lives.

Our mission is focused and our way forward is clear. I thank Chairman Pitts, Ranking Member Pallone and Members of the Subcommittee for the opportunity to testify today, and to share Edwards' experience in delivering an important new therapy to U.S. patients in need. I applaud the work you are doing with the 21st Century Cures initiative to ensure that U.S. patients continue to benefit from the amazing innovations being developed close to home. We welcome your support to remove the barriers that may prevent patients like Lester from accessing therapy that, in the words of some wise physicians, puts more years in their life, and more life in their years.