June 2, 2011
Congressional Hearing

Thank you Chairman Gowdy, Ranking Member Davis and other distinguished members of the House Oversight and Government Reform Subcommittee for inviting me to submit testimony on medical devices at this important hearing. I am Rita Redberg, MD, MSc, Professor of Medicine and full-time Faculty Member in the Division of Cardiology at the University of California, San Francisco Medical Center for 21 years. I am Director of our Women's Cardiovascular Service. I am also the chief editor of the *Archives of Internal Medicine*, one of the most preeminent peer-reviewed journals of scientific research in internal medicine. I am a member of the FDA Cardiovascular Device Expert Panel. Much of my own research has concerned the appropriate and optimal use of medical devices in patient care, and the journal frequently publishes articles related to use of medical devices.

As a practicing cardiologist, I appreciate the advantages that medical devices offer in care of my patients every day. I also know the problems and heartache that can occur when an implanted device is found not to be effective or has been found to be defective and is recalled. My first priority is high quality medical care of my patients. Thus, it is critical to me that any approved high-risk device has FIRST been shown to be safe and effective. Unfortunately, this standard too frequently is not currently met. First, *only 1%* of all devices go through the pre-market approval pathway. Congress envisioned that all Class III devices (those with greatest risk) would be approved through the more rigorous pre-market approval (PMA) process. However, the 2009 GAO report entitled FDA *Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process* found that this Congressional directive was not being followed. The report found that the majority of high-risk devices do not go through the original PMA process, and instead are commonly approved with no clinical study data. Class III devices are defined by the FDA as "usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury." Of over 10,000 submissions for Class II devices that FDA cleared via the 510(k) process, the GAO found that "over one -quarter were for devices that were implantable: were life sustaining; or presented significant risk to the health, safety or welfare of a patient" and thus should have gone through the PMA process. Even, the PMA process has been found to need improvement in its clinical data requirements. Our recent study published in JAMA found that fully two-thirds of PMA cardiovascular devices were approved on the basis of only a single study. Moreover, only 27% of those studies were randomized and only 14% were blinded, and only half had a comparison control group. Thus, the majority of these high-risk implanted devices were approved without the support of high quality data on safety and effectiveness.

For example, as chronicled in the *Chicago Tribune* last week, the Myxo valve, an annuloplasty ring permanently implanted as a heart valve replacement, was approved through a 510(k) process. This valve clearly falls within the FDA definition for a Class III device and was originally classified as such by FDA. However, according to the

Tribune, the FDA "rubber-stamped" the device industry's request to reclassify from Class III to Class II in 2001. The petition for reclassification cited studies finding that the rings were safe and effective, however, none of these studies were randomized clinical trials. Furthermore, many of the study investigators were heart surgeons who invented the devices and were receiving royalties from the manufacturer. These relationships were not revealed to the patients who received these annuloplasty rings. Moreover, Edwards had sold the device for two and a half years without 510(k) clearance, after the company determined from an FDA document that a new 510(k) wasn't needed. However, shortly after press reports on this lack of FDA clearance, the company submitted a new 510(k), and the FDA ultimately cleared the device in April 2009. There were no penalties to Edwards Lifesciences for this infraction. In the most recent 5-year period, there have been more than 3,400 adverse events reported involving annuloplasty rings and these rings have been linked to just 56 fewer deaths than heart replacement valves, yet the annuloplasty ring went through a 510(k) clearance without the benefit of clinical trials. This number is especially disturbing, as it is estimated that only 5% of all adverse events are even reported. Adverse event reporting is voluntary for hospitals and doctors. Manufacturers are required to report deaths and injuries. However, there are an unknown number of delays in adverse event reporting by the manufacturer. For example, last April, an **FDA** inspection of medical-device maker Edwards Lifesciences identified six complaints of adverse events relating to use of mitral annuloplasty rings and pericardial prosthetic heart valves that were not reported to the FDA within the required 30-day window.

There is also room for improvement in the completeness of the data collected and reported by the FDA on approved devices. Our recent study published in *Circulation: Quality and Outcomes*, which reviewed Gender Bias in PMA cardiovascular devices, we found that nearly one-third of FDA studies did not report sex of the enrollees, and only 41% contained the required gender bias analysis confirming that data evaluated effectiveness in both men and women. A recent meta-analysis of implantable cardiac defibrillators (ICD) found that randomized trials showed no mortality benefit of ICDs in women, yet these devices have been routinely implanted in women for more than a decade despite the lack of evidence of benefit in women.

After FDA approval, Medicare and private insurance coverage often immediately follows and use generally expands. For example, drug coated stents, approved in 2003, meteorically shot to 90% of all stents used. The vast majority of usage was and remains off-label, e.g. not for FDA approved indications. A recent study found that use of such stents has added as much as $1.6 billion to Medicare costs since their introduction. Yet studies show that approximately one-third of these devices are implanted in persons who have never been shown to benefit from their use, such as persons without any symptoms.

The FDA is sorely underfunded for its enormous mission of protecting the public health by assuring food and drug and device safety. FDA device review is partially supported by industry user fees, Currently, device user fees are lower than pharmaceutical user fees even though drug trials are much more expensive to conduct than device trials. The FDA charged a standard fee of $4,007 for a 510(k) submission (and only half that amount for

small companies) and $217,787 for an original PMA (one-quarter that amount for small companies), compared to $702,750 to $1,405,500 for prescription drug applications according to 2010 data. The PMA user fees provide less than one-fourth of the $870,000 average cost of the review in terms of FDA staff and resources, creating a disincentive for FDA to select the PMA process. Increasing the budget of the Center for Devices and Radiologic Health would help to speed up device approvals by allowing more FDA staffers to review applications more expeditiously. But the process cannot and should not be speeded up by foregoing the requirement data of safety and effectiveness.

Technology is widely agreed to be the #1 reason for rapidly increasing health care costs and rapidly rising premiums, which threaten the stability of many US businesses. The medical device industry is over $100 billion per year. That is a good investment when such devices have been shown to be beneficial. But too often in the US we do not have this assurance of patient benefit before FDA approval.

The US device approval process often is compared to the European medical regulatory system. A recent review in the *BMJ* found that while European conditions may be more favorable for industry, they are not necessarily best for patients. The decision making process in Europe occurs "behind closed doors" and there is no publicly available summary for the reason for granting a CE mark. The BMJ editors contacted 192 manufacturers to request evidence of the clinical data used to approve their devices in Europe and every one denied access, stating "clinical data is proprietary information". The UK regulator expressed concerns about their current system, stating, "the evidence on safety and efficacy of new devices and new procedures at the time they are introduced into the UK practice is very variable," and noting that the evidence base for most devices was poor.

True innovations are welcomed, but cannot be recognized as such without clinical trial evidence to show that new technologies are beneficial for patients. Only high-quality clinical trials can assure safety and benefit, especially for invasive devices, from which patients incur risk of infection, bleeding and even death. It is well worth the time up front to gather data of safety and effectiveness so that my fellow cardiologists and I can confidently tell our patient that implantation of a device is in their best interest.