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## Postmarketing Surveillance of Medical Devices — Filling in the Gaps

Frederic S. Resnic, M.D., and Sharon-Lise T. Normand, Ph.D.

Failures of implantable medical devices, although rare, can carry a substantial risk of serious injury. From 2000 through 2011, more than 150 new high-risk medical devices were approved by the Food and Drug Administration (FDA) through the premarket approval (known as PMA) process, and an additional 600 devices were cleared through the less demanding 510(k) process, in four medical specialty areas (cardiovascular care, neurology, obstetrics and gynecology, and orthopedics; see graph). The problem that Hauser describes (pages 873–875) — the erosion of the insulation in St. Jude Medical's Riata leads for implantable cardioverter-defibrillators — highlights the fact that medical devices are complex assemblies of multiple components, and the failure of any single component can lead to unexpected and serious safety problems. Because it is impossible to design an implantable medical device with zero risk of failure, effective systems for monitoring safety after a device is on the market are essen-


tial for protecting the public health. Moreover, since incremental changes are made in medical devices throughout their life cycles, it is impractical to prospectively study each change comprehensively before marketing. Balancing the need for robust postmarketing safety monitoring with the need to avoid the stifling of innovation is a prime responsibility of the Center for Devices and Radiological Health (CDRH) at the FDA.

The FDA's safety-surveillance strategy has relied on physicians, health care institutions, manufacturers, and patients to report medical device failures and complications through the Medical Device Reporting system. This system can identify unanticipated medical device failures and complications but requires extensive analytic review and has important limitations.<sup>1</sup> Although the CDRH receives more than 100,000 reports annually, the proportion of medical device failures that are registered is estimated to be less than 0.5%; this low reporting rate greatly limits the information available regarding the balance of risk and health improvement associated with a given medical device.<sup>2</sup>

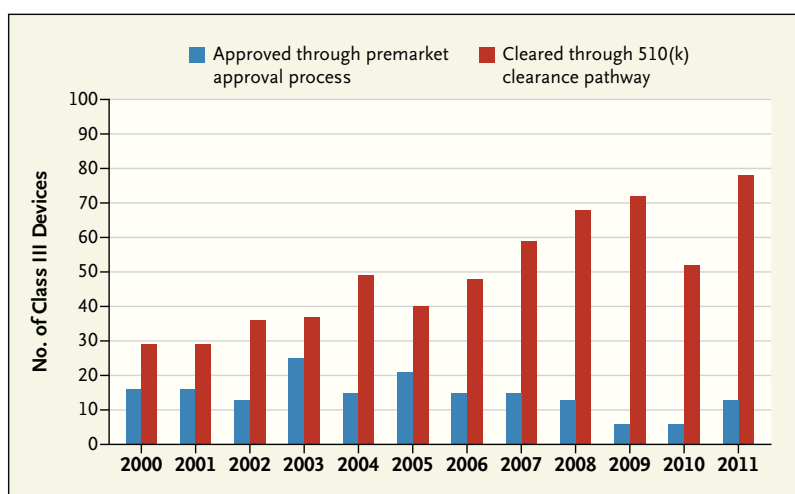
Several FDA initiatives have been launched to fill the gaps in

the passive event-reporting system. In 2002, the CDRH established the Medical Product Safety Network, which represents more than 300 health care institutions that collaborate to identify and investigate trends in device failures and adverse events. In 2007, the FDA was given the regulatory authority to mandate follow-up safety studies after initial market approval (the Section 522 rule) — a change that improves the agency's flexibility to investigate potential safety concerns. In 2009, the FDA launched the Sentinel initiative, a program to integrate the electronic health records of large, representative U.S. populations for postmarketing safety analysis. However, despite great success in linking nearly 100 million claims-based health records, Sentinel projects have thus far focused only on medications — at least in part because of the very limited information about medical devices currently available in billing claims data.

In contrast to drugs, medical devices suffer from a major impediment to safety monitoring: the lack of unique device identifiers (UDIs). To address this lim-

 An audio interview with Prof. Normand is available at NEJM.org

tial for protecting the public health. Moreover, since in-



**Numbers of High-Risk (Class III) Medical Devices Approved or Cleared by the FDA in Cardiovascular Care, Neurology, Obstetrics and Gynecology, and Orthopedics, 2000–2011.**

The proportion of class III devices introduced through the 510(k) clearance pathway, which generally requires little clinical premarketing testing, has increased significantly during the past decade. Therefore, effective and efficient postmarketing surveillance has become ever more important. Data are from the FDA.

itation, the FDA Amendments Act of 2007 authorized the agency to develop a comprehensive UDI system, which is currently under review within the Office of Management and Budget. As a UDI system is integrated with administrative and claims databases, it will become possible to identify patients who have been exposed to specific devices. However, the complex interplay among device design, the procedural safety of implantation, the learning curve associated with medical devices, and the risks to individual patients will continue to make it difficult to conduct effective and reliable safety surveillance using only billing data.

There are important opportunities to leverage large, disease-specific clinical registries for monitoring device safety. In many countries, such registries are a mandatory component of the health care system and required for all implantations of high-risk devices. In the United States, there is no national system to

ensure that registries exist for high-risk medical devices. Nevertheless, several nonprofit professional medical organizations in the United States have recognized the critical need for medical device registries and have spearheaded their development in an effort to monitor and improve the quality of care. The American College of Cardiology, in conjunction with several partner organizations, has established detailed clinical registries covering many high-risk cardiovascular devices, including coronary stents, implantable defibrillators, and defibrillator leads, which together contain information on approximately 4 million implantation procedures. The recently developed transcatheter heart-valve registry will provide early postmarketing information about the safety of this revolutionary treatment for patients with high-risk aortic-valve stenosis. Clinical registries in cardiac surgery already exist, and newer efforts by professional societies related to

orthopedics, ophthalmology, and other fields are under way.

Perhaps the most successful example of a coordinated effort to study newly introduced devices has been the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), established to capture detailed clinical data on all patients receiving implantable ventricular assist pumps in the United States. Its success is related to the requirement by the Centers for Medicare and Medicaid Services (CMS) that patient information be entered into an audited national registry as a condition of reimbursement. INTERMACS now serves as a ready infrastructure to support the postapproval study of every new generation of mechanical cardiac support device, saving manufacturers substantial time and resources that they would otherwise have to invest in establishing new systems of data collection, auditing, and analysis.<sup>3</sup>

Creating and maintaining these detailed clinical registries is challenging and expensive. Many registries are supported by voluntary submissions from health care providers, so hospitals must bear the costs of collecting and submitting information. Emerging standards for electronic health records, including “meaningful use” regulations, will provide unprecedented opportunities for securely mapping clinical information to distributed clinical registries.

But having reliable and complete clinical data is not enough. The development of sound methods and practical tools for monitoring safety over a product’s life cycle is essential. We have advocated a strategy of automated prospective surveillance of high-risk implantable devices, using

database monitoring tools to support continuous surveillance of clinical registries.<sup>4</sup> Such tools are capable of monitoring hundreds of high-risk medical devices simultaneously, to maximize efficiency in detecting unrecognized safety problems. Automated surveillance systems constantly watch a growing database of clinical experience and trigger an alert when the rate of a device failure or complication rises above threshold levels. Automated monitoring tools must incorporate the best available statistical methods to account for the complexity of the surveillance of device safety, including risk differences among patients, effects of physicians' learning curves, and interactions between the device and medications; they must also balance specificity and sensitivity in the detection of safety signals to permit efficient epidemiologic exploration of such alerts.

The complexity of device-safety surveillance requires the use of complementary approaches in an organized, prospective strategy. A comprehensive national safety surveillance system must include

several key elements, beginning with the adoption of the proposed UDI system. We recommend expedited review and finalization of the UDI rule to permit implementation as soon as possible. Next, the FDA, together with the CMS, should require that detailed information regarding the use of high-risk devices and clinical outcomes be submitted to selected national registries operated by independent academic or professional medical organizations. We recommend that the FDA retain full rights of access to the data for additional analysis as needed. Third, the FDA should redirect a portion of the resources currently spent by the medical device industry on underpowered condition-of-approval studies to support the national device-safety registries. Fourth, automated safety-surveillance tools should be applied to device registries to prospectively monitor for the most severe and the most common device failures and complications. Finally, methods for linking information across pre-marketing studies, the new registries, and existing FDA surveillance systems to provide valid

safety estimates require further development.

Complementing existing event-reporting systems with enhanced prospective surveillance of high-quality registries will permit the FDA to efficiently monitor the safety of increasingly complex and widely used medical devices.

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## Why Now Is Not the Time for Premium Support

Henry J. Aaron, Ph.D., and Austin B. Frakt, Ph.D.

The United States faces large and growing federal budget deficits, driven in substantial measure by the projected growth of Medicare spending. Recently, various groups have proposed solutions they call “premium support” or “defined support.” A study panel of the Bipartisan Policy Center, chaired by former senator and budget committee chair Pete Domenici (R-NM) and

Alice Rivlin, former director of the Office of Management and Budget and the Congressional Budget Office, proposed one variant. Senator Ron Wyden (D-OR) and Representative Paul Ryan (R-WI) proposed a similar plan.

These proposals would offer Medicare beneficiaries vouchers toward the purchase of private insurance or traditional Medicare. Private-plan offerings could vary,

but the actuarial value of these alternatives would have to be at least equal to that of traditional Medicare. Increases in the amount of the voucher would be capped by an index that is expected to rise more slowly than health care costs. Advocates claim that cost-conscious enrollees and competition among profit-seeking insurers would hold down program costs. But if they didn't, the growth cap