

CORRESPONDENCE



Medical-Device Safety and the FDA

TO THE EDITOR: In his Perspective article, Maisel (March 6 issue)¹ criticizes the response of the Food and Drug Administration (FDA) to adverse events preceding the recall of Medtronic's Sprint Fidelis implantable cardioverter-defibrillator (ICD) leads. The FDA agrees with Maisel's premise that physicians and patients should receive accurate and timely information about problems with marketed medical devices. In fact, we are increasing our efforts to issue early communications about potential problems with regulated medical products, and we have created a new Risk Communication Advisory Committee to help us do so. However, we are concerned about several statements in Maisel's article that may have misled readers.

For example, Maisel criticizes the FDA for approving changes in the Medtronic lead on the basis of bench testing rather than clinical data. FDA regulations allow manufacturers to apply for marketing of a modified device on the basis of

bench testing, and many devices are approved in this way. This is not an inherently unsafe approach, as Maisel implies. In evaluating an application involving a modified device, we analyze the proposed modification, determine the potential types of failure, and tailor testing requirements accordingly. In many cases, our questions are best answered by performing appropriate engineering analyses, but in other cases, we also require clinical data.

To require that these modified devices undergo clinical trials across the board as a condition of FDA approval would limit the availability of improved products. Also, most of these trials would have insufficient power to detect small but clinically meaningful differences in performance.

Maisel also criticizes device manufacturers for continuing to market existing models while modified (and presumably improved) models await FDA approval. But there is nothing inherently wrong with doing so unless the older models pose an undue health risk. The continued marketing of Fidelis leads occurred when available data indicated that the fracture rate was similar to that of other leads. When continued monitoring of the situation showed otherwise, the lead was recalled and existing stocks were promptly called back.

Unfortunately, Maisel's article diverts attention from deeper problems. For example, how can bench testing be better designed to be predictive of clinical performance? How can postmarketing clinical registries be used more effectively as early warning systems, alerting us to low-frequency, unexpected problems with devices? And given that we cannot detect low-rate events without a steady flow of accurate information, how can physicians be persuaded to report adverse events to us promptly? We welcome thoughtful input on

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these issues from clinicians, patients, and the medical-device industry.

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1. Maisel WH. Semper fidelis — consumer protection for patients with implanted medical devices. *N Engl J Med* 2008;358:985-7.

THE AUTHOR REPLIES: Because of their inherent complexity and widespread distribution, medical devices will occasionally malfunction, fail, or cause unexpected adverse events. It is challenging to predict the long-term performance of implanted devices on the basis of bench testing or pre-marketing clinical trials of short duration. Thus, for selected life-sustaining products, postmarketing studies of sufficient size and duration must be required of manufacturers. Unfortunately, when questions first arose about the performance of the Medtronic Sprint Fidelis ICD lead, the available postmarketing data were insufficient

to allow an accurate evaluation of the device's performance. Over the ensuing months, tens of thousands of additional patients underwent implantation of the lead, only to be notified of its recall a short time later.

There is no “deeper” problem than the unnecessary exposure of patients to an underperforming permanently implanted medical device. Schultz outlines several important questions that must be answered in order to strengthen the device-approval and postmarketing-monitoring processes. In addition, technological advances such as remote, wireless device monitoring will, in some cases, facilitate collection of the needed performance data. More critical, however, is the need for a philosophical shift — from a medical-device industry that primarily reacts to performance failures to one that better anticipates them.

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Mechanical Ventilation and Disuse Atrophy of the Diaphragm

TO THE EDITOR: In their article, Levine et al. (March 27 issue)¹ conclude that atrophy of the human diaphragm occurs with mechanical ventilation; this finding is consistent with our observation of atrophy of the diaphragm in a patient with a high spinal cord injury after 8 months of mechanical ventilation necessitated by the failure of one diaphragmatic pacemaker.² In this patient, atrophy of the diaphragm was prevented in the hemidiaphragm connected to the functioning pacemaker by stimulating the pacemaker for only 30 minutes per day. Levine et al. speculate as to whether there are functional implications due to atrophy and whether strategies can be used to prevent atrophy. Our study addresses both of these questions. First, we found that atrophy was associated with profound reductions in tidal volume. Second, we found that stimulation of the phrenic nerve of the diaphragm for 30 minutes per day was sufficient to prevent atrophy. From our observations and those of Levine et al., one major question arises: Is the diaphragmatic activation associated with the forms of ventilation

commonly used in the intensive care unit sufficient to prevent disuse atrophy?

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1. Levine S, Nguyen T, Taylor N, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med* 2008;358:1327-35.
2. Ayas NT, McCool FD, Gore R, Lieberman SL, Brown R. Prevention of human diaphragm atrophy with short periods of electrical stimulation. *Am J Respir Crit Care Med* 1999;159:2018-20.

TO THE EDITOR: Levine and colleagues confirm that in the absence of respiratory effort, mechanical ventilation for as little as 1 day causes profound atrophy of the diaphragm in adult humans, as it does in animals. Two decades ago, Knisely