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"The Danger Within Us"

By Jeanne Lenzer, 2017, 329 pages, Little, Brown and Company, $28.00

Review by Norman M. Goldfarb

"The Danger Within Us" provides a 500-volt wake-up call for the medical device industry and its regulators that should not be ignored. Every couple of years, the biopharmaceutical industry has to deal with an exposé. With the publication of this book on implantable devices, the device industry no longer has to feel left out.

How well does the FDA's current medical device process serve the public? The following extracts from the book (source citations excluded) might help you decide:

> Despite claims by the FDA that high-risk implanted medical devices have to undergo "rigorous premarket testing," the agency requires clinical testing for only a small fraction of high-risk devices… In 2001, the agency approved 71 devices via the PMA pathway. In 2005, the number dropped to 43. By 2009, only 20 devices were approved via the PMA pathway.
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> The 1976 Medical Device Amendments were intended to ensure that high-risk devices would undergo scientifically valid clinical testing. Yet, three decades later, only 16% (170 of 1,062) of the highest-risk devices approved by the FDA had gone through the PMA process. The rest had been either cleared without clinical testing through the 510(k) process (21%) or approved by supplemental filing (63%). Of the latter, only 0.3% were required to provide clinical data.
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> Even when devices did undergo clinical testing, a 2009 study of 78 applications for high-risk cardiovascular devices found that only 27% of studies (33 of 123) were randomized, only 14% were blinded, 88% of the primary end points were surrogate markers, roughly half of the studies had no control group, and nearly a third of those that did were retrospective — a form of review that is generally not as scientifically sound as a randomized controlled trial.
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> In 2015, approximately 16,000 deaths associated with medical devices were reported to the FDA. A Government Accountability Office analysis found that 99% of device-related "adverse events" are never reported to the FDA and that the "more serious the event, the less likely it was to be reported." Based on the GAO analysis, that means medical devices could have been associated with as many as 1.6 million deaths in 2015. Even if only 1% to 10% of those deaths were *caused* by a device, that means between 16,000 and 160,000 people may have been killed by devices, making medical devices one of the leading causes of death in the U.S.
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> One study found that, of 113 device recalls initiated because of a risk of serious injury or death, only 19% had been approved through the PMA process, meaning that 81% of devices that caused the worst harm were cleared or approved through pathways that didn't require clinical testing by the FDA.
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> The Supreme Court ruling on preemption [of manufacturer liability] presupposes that the approval process is bulletproof and provides sufficient protection to the public. If that were the case, the FDA would not have to recall about 1,100 devices annually. A number of recalls are "class 1" recalls, which, according to the FDA, means there is "a reasonable probability" that the recalled device could "cause serious adverse health consequences or death." …As devices become increasingly complex and

> invasive, the number of class 1 recalls has been rising year after year: In 2003, there were eight class 1 recalls; that number rose to 176 in 2013.

The book focuses on one epilepsy patient's harrowing journey with the Cyberonics implanted device for vagus nerve stimulation (VNS). It is a horrific story that appears to have brought out the worst in our current system, and it should be required reading for anyone considering VNS.

Should FDA have approved the Cyberonics VNS device? The following extracts from the book might help you decide:

> A further clue that the VNS device might not have any real efficacy was buried in the company's 1997 physician manual (Cyberonics did not present these data during the 1997 [FDA] hearing). In a review of what happened after a patient's VNS device stopped delivering shocks because of battery depletion, of 72 patients, 15% had more seizures, while 58% percent had fewer seizures. In other words, patients were far more likely to do better rather than worse when the VNS device stopped working.
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> Twelve years after the device was approved for epilepsy, the company hadn't collected death data for the five studies submitted as proof of safety and wouldn't release the death data it did collect outside the studies. I informed the FDA, assuming that the company would get slammed by the regulator for failing to collect death data on a device approved only conditionally because of the FDA's concerns about a "high rate of deaths." But the FDA continued to insist the device was safe. When I pressed the agency about this, it responded in an email that it hadn't asked the company to count the number of deaths; instead, it only required Cyberonics to "characterize mortality." I wondered: How does one *characterize* mortality without knowing whether anyone implanted with the device *died*?

The book describes serious problems with a few other devices and then, halfway through the next-to-last chapter, turns to a mini-exposé of a Genentech's drug, tPA. While a fascinating and disheartening story, are there really no other problematic devices to crush?

The last chapter sums up the problems, including industry venality, the financial seduction of physicians and academia, and multiple FDA deficiencies: lack of resources, incompetence, opacity, politicization and the shoddy MAUDE adverse-event database. For solutions, it recommends independent clinical trials by unbiased third-parties, ending the Bayh-Doyle Act, dispensing with patents, single-payer healthcare, and social justice to address the roots of the healthcare problems in the U.S. Good luck with that…

The book's author, Jeanne Lenzer, is a well-regarded and relentless investigative journalist. The industry will probably keep its head down, as usual, and not respond with persuasive rebuttals and/or a plan to address the issues, but we really need to take this book seriously.

The book includes 12 chapters:

- Strange Seizures
- Age of Miracles
- Deadly Devices
- The Man from Cyberonics
- Adverse Events
- No Safety Net
- Regulators in Chains
- The Power of Illusions
- The Quest for Truth

- When Money Talks
- Breakdown
- What Is to Be Done?

Reviewer

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